

Hanley
081882499

08/882499

=> fil reg

FILE 'REGISTRY' ENTERED AT 16:48:39 ON 03 JUN 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 1999 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 28 MAY 99 HIGHEST RN 223764-44-1
DICTIONARY FILE UPDATES: 03 JUN 99 HIGHEST RN 223764-44-1

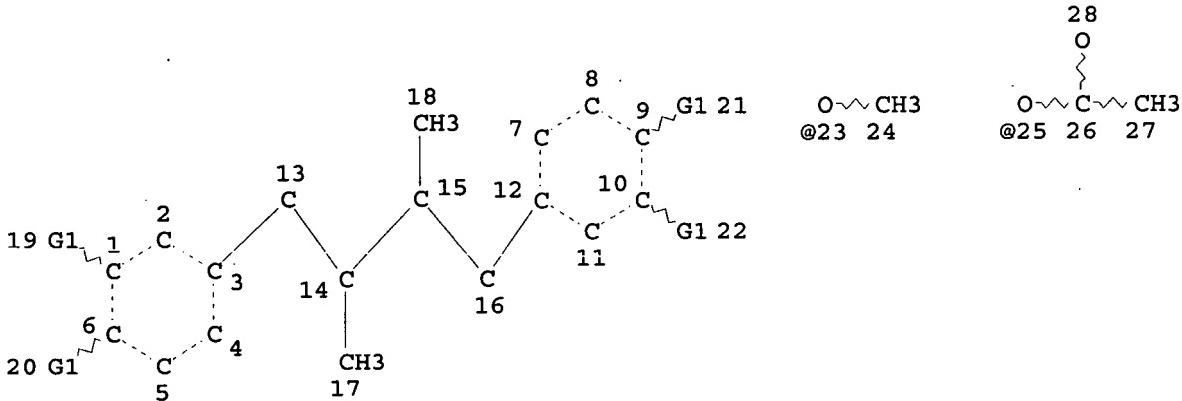
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

=> d que stat

Str.

L5 STR



VAR G1=OH/23/25

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE

L7 162 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED 8418 ITERATIONS

162 ANSWERS

SEARCH TIME: 00.00.02

Searcher : Shears 308-4994

08/882499

=> s 17 and 1/nc

L8 16251359 1/NC
 147 L7 AND 1/NC

=> d his 19- ful; sel hit l12 1-29 rn

(FILE 'CAPLUS' ENTERED AT 16:48:52 ON 03 JUN 1999)
L9 1063 SEA ABB=ON PLU=ON L8 OR L8/D
L10 6 SEA ABB=ON PLU=ON L9 AND (VIR?(3A)GROW? OR (HSV OR
 HV) (S)HERPES? OR HERPES?)
L11 28 SEA ABB=ON PLU=ON L9 AND (ANTIVIR? OR VIRAL? OR
 VIRUS?)
L12 29 SEA ABB=ON PLU=ON L10 OR L11

E1 THROUGH E37 ASSIGNED

=> d 1-29 ibib abs hitstr; fil reg

L12 ANSWER 1 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1999:244515 CAPLUS
DOCUMENT NUMBER: 130:276777
TITLE: Nontoxic extract of Larrea tridentata,
 production method, and therapeutic use
INVENTOR(S): Sinnott, Robert A.
PATENT ASSIGNEE(S): Larreacorp, Ltd., USA
SOURCE: PCT Int. Appl., 58 pp.
 CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917609	A1	19990415	WO 98-US19817	19980914
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
WO 9815184	A1	19980416	WO 97-US18103	19971007
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,			
			Searcher : Shears	308-4994

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, UA, UG, US, UZ, VN, YU, ZW

PRIORITY APPLN. INFO.:

WO 97-US18103	19971007
US 97-64674	19971020
US 97-64802	19971020
US 97-64803	19971020
US 97-64804	19971020
US 97-64805	19971020
US 96-726686	19961007

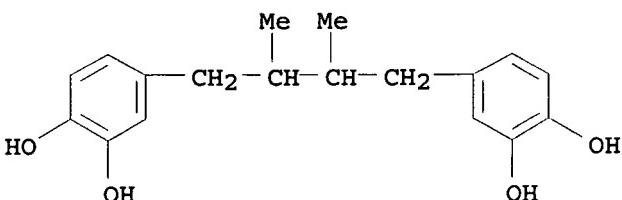
AB A nontoxic, therapeutic agent having pharmacol. activity comprising concd. ext. of Larrea tridentata plant material and ascorbic acid is made by a process in which the plant material is extd. using an org. solvent, and is then satd. with ascorbic acid to reduce the toxic NDGA quinone, which naturally occurs in the plant material, to NDGA itself. Addnl. amts. of ascorbic acid are added to the ext. to inhibit the natural oxidn. of the NDGA into the toxic NDGA quinone in vivo, or during processing or storage. The resulting ext. is useful in the treatment of viral diseases caused by viruses from the Herpesviridae family or viruses which require the Sp1 class of proteins to initiate viral replications. The resulting compd. can also be used as an antiinflammatory when the inflammatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize NDGA as a therapeutic agent or a food additive.

IT 500-38-9P, Nordihydroguaiaretic acid

RL: BAC (Biological activity or effector, except adverse); FFD (Food or feed use); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Larrea tridentata nontoxic ext., prodn. method, combinations with other agents, and therapeutic use)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



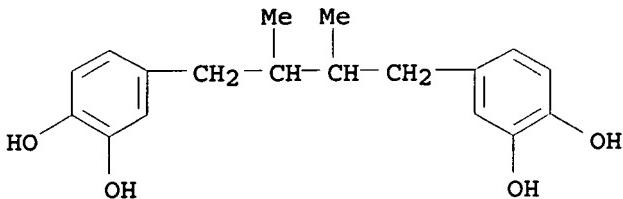
IT 500-38-9D, Nordihydroguaiaretic acid, oxidn. products

RL: RCT (Reactant)
(Larrea tridentata nontoxic ext., prodn. method, combinations with other agents, and therapeutic use)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA Searcher : Shears 308-4994)

INDEX NAME)



L12 ANSWER 2 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1998:601918 CAPLUS

DOCUMENT NUMBER: 129:310451

TITLE: Human immunodeficiency **virus** type 1
cDNA integration: new aromatic hydroxylated
inhibitors and studies of the inhibition
mechanismAUTHOR(S): Farnet, C. M.; Wang, B.; Hansen, M.; Lipford, J.
R.; Zalkow, L.; Robinson, W. E., Jr.; Siegel,
J.; Bushman, F.CORPORATE SOURCE: Salk Institute for Biological Studies, La Jolla,
CA, 92037, USASOURCE: Antimicrob. Agents Chemother. (1998), 42(9),
2245-2253

CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Integration of the HIV-1 cDNA is a required step for viral replication. Integrase, the **virus**-encoded enzyme important for integration, was not yet exploited as a target for clin. useful inhibitors. Here we report on the identification of new polyhydroxylated arom. inhibitors of integrase including ellagic acid, purpurogallin, 4,8,12-trioxatricornan, and hypericin, the last of which is known to inhibit viral replication. These compds. and others were characterized in assays with subviral preintegration complexes (PICs) isolated from HIV-1-infected cells. Hypericin was found to inhibit PIC assays, while the other compds. tested were inactive. Counterscreening of these and other integrase inhibitors against addnl. DNA-modifying enzymes revealed that none of the polyhydroxylated arom. compds. are active against enzymes that do not require metals (methylases, a pox **virus** topoisomerase). However, all were cross-reactive with metal-requiring enzymes (restriction enzymes, a reverse transcriptase), implicating metal atoms in the inhibitory mechanism. In mechanistic studies, we localized binding of some inhibitors to the catalytic domain of integrase by assaying competition of binding

Searcher : Shears 308-4994

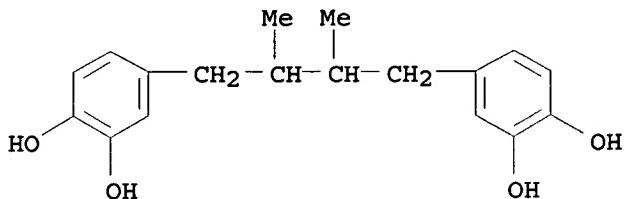
by labeled nucleotides. These findings help elucidate the mechanism of action of the polyhydroxylated arom. inhibitors and provide practical guidance for further inhibitor development.

IT 500-38-9, Nordihydroguaiaretic acid

RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (inhibition activity and mechanism of arom. hydroxylated inhibitors for HIV-1 cDNA integration tested on preintegration complexes)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 3 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1998:484927 CAPLUS

DOCUMENT NUMBER: 129:127177

TITLE: Pharmaceutical preparations of glutathione and methods of administration

INVENTOR(S): Demopoulos, Harry B.; Seligman, Myron L.

PATENT ASSIGNEE(S): Antioxidant Pharmaceuticals Corp., USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9829101	A1	19980709	WO 97-US23879	19971231
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9856205	A1	19980731	AU 98-56205	19971231
		Searcher : Shears		308-4994

08/882499

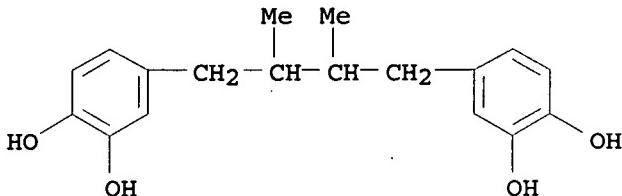
PRIORITY APPLN. INFO.: US 96-34101 19961231
WO 97-US23879 19971231

AB A method of increasing glutathione levels in mammalian cells comprises administering an oral bolus of encapsulated pharmaceutically stabilized glutathione in a rapidly dissolving formulation to a mammal on an empty stomach. Pharmaceutical formulations including glutathione are also disclosed.

IT 500-38-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (glutathione pharmaceutical preps. and methods of administration)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 4 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:450910 CAPLUS
DOCUMENT NUMBER: 129:197598
TITLE: Antiviral Activities of Methylated Nordihydroguaiaretic Acids. 2. Targeting Herpes Simplex Virus
AUTHOR(S): Chen, Hongshan; Teng, Li; Li, Jian-Nong; Park, Richard; Mold, David E.; Gnabre, John; Hwu, Jih Ru; Tseng, Wen Nan; Huang, Ru Chih C.
CORPORATE SOURCE: Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences, Beijing, Peop. Rep. China
SOURCE: J. Med. Chem. (1998), 41(16), 3001-3007
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We had previously reported that tetramethyl-O-NGDA (M4N), a synthetic deriv. of the naturally occurring nordihydroguaiaretic acid (NDGA), is able to inhibit HIV Tat transactivation by blocking host Sp1 protein at the Sp1 cognate binding site on the HIV LTR promoter. The present studies were undertaken to examine whether

Searcher : Shears 308-4994

M4N is able to inhibit the replication of **herpes simplex virus (HSV)**, another Sp1-regulated virus

The results showed that in Vero cells, M4N inhibits at micromolar levels ($IC_{50} = 43.5 \mu M$) the expression of the **herpes immediate early gene (.alpha.-ICP4)**, which is essential for HSV replication. An electrophoretic mobility shift assay, examg. Sp1 binding to the **.alpha.-ICP4 promoter**, showed a significant inhibition of the control bands: 88% inhibition of the fast moving band (FMB) and 45% of the slow moving band (SMB), at 100 μM of drug concn. Comparative studies between M4N and acycloguanosine (acyclovir, ACV) in cultured Vero cells revealed an interesting pattern in the drug sensitivity (IC_{50}) and cytotoxicity (TC_{50}) parameters. For M4N, the IC_{50} varied between 11.7 and 4 μM in 10 passages of HSV-1 and 4 passages of HSV-2 with no indication for a requirement of higher drug concn. In contrast, for acyclovir, the IC_{50} increased from 7 μM in the first passage to 444 μM in the tenth passage of HSV-1, and >88 μM for the fourth passage of HSV-2, indicating a rapid build-up of drug resistance against acyclovir. While the selective index (SI), defined as the ratio: TC_{50}/IC_{50} , remained relatively const. for M4N; it dropped 60-fold for acyclovir in the endpoints of viral passages. Drug sensitivity for M4N toward the acyclovir-sensitive strain (sm44) and the acyclovir-resistant strain (ACV-10) of HSV-1 was similar, indicating no cross-resistance between M4N and acyclovir in their anti-HSV effects. These results may have an important clin. relevance since HSV has been shown to be a factor for spreading of HIV.

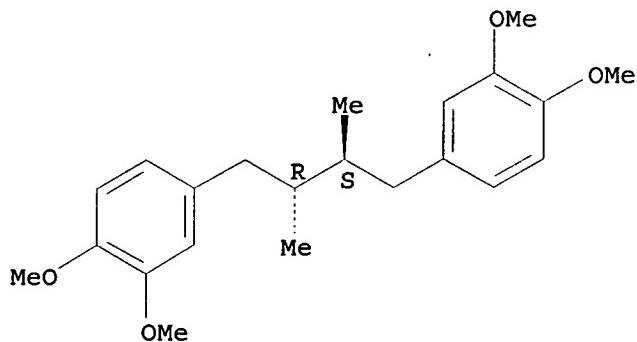
IT 24150-24-1

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (targeting **herpes simplex virus** replication
 by mutation-insensitive transcription inhibitor
 tetra-O-methyl-NDGA)

RN 24150-24-1 CAPLUS

CN Benzene, 1,1'-(2,3-dimethyl-1,4-butanediyl)bis[3,4-dimethoxy-,
 (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L12 ANSWER 5 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1998:450908 CAPLUS

DOCUMENT NUMBER: 129:216452

TITLE: Antiviral Activities of Methylated Nordihydroguaiaretic Acids. 1. Synthesis, Structure Identification, and Inhibition of Tat-Regulated HIV Transactivation

AUTHOR(S): Hwu, Jih Ru; Tseng, Wen Nan; Gnabre, John; Giza, Paul; Huang, Ru Chih C.

CORPORATE SOURCE: Organosilicon and Synthesis Laboratory
Department of Chemistry, National Tsing Hua University, Hsinchu, 30043, TaiwanSOURCE: J. Med. Chem. (1998), 41(16), 2994-3000
CODEN: JMCMAR; ISSN: 0022-2623

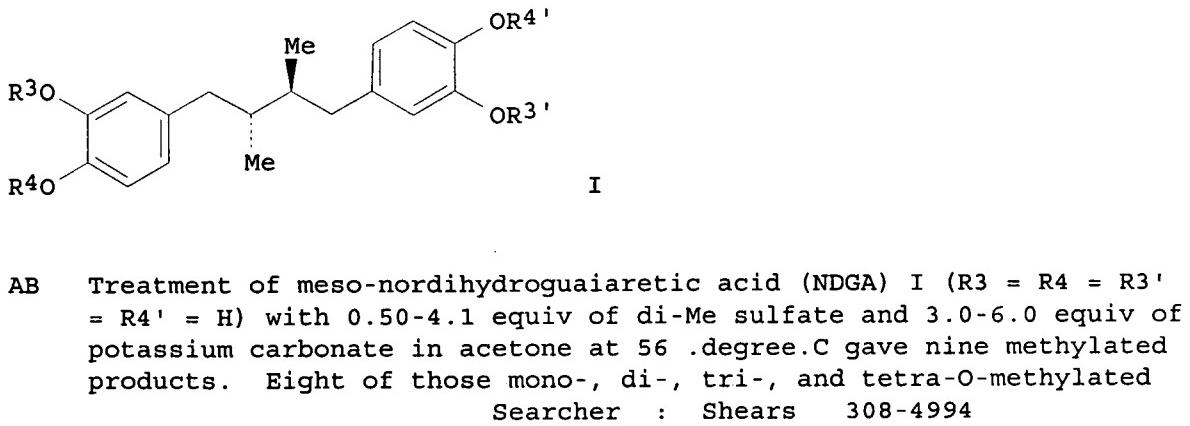
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 129:216452

GI



AB Treatment of meso-nordihydroguaiaretic acid (NDGA) I ($\text{R}^3 = \text{R}^4 = \text{R}^3' = \text{R}^4' = \text{H}$) with 0.50-4.1 equiv of di-Me sulfate and 3.0-6.0 equiv of potassium carbonate in acetone at 56 .degree.C gave nine methylated products. Eight of those mono-, di-, tri-, and tetra-O-methylated

Searcher : Shears 308-4994

08/882499

NDGAs were isolated in pure form, and their structures were identified unambiguously by spectroscopic methods. A preparative amt. of tetra-Me NDGA I ($R_3 = R_4 = R_3' = R_4' = \text{Me}$) was obtained in 99% yield from NDGA by use of 4.1 equiv of di-Me sulfate for the methylation. Among the eight different methylated NDGAs, I ($R_3 = R_4 = R_3' = R_4' = \text{Me}$) showed the strongest anti-HIV activity ($\text{IC}_{50} 11 \mu\text{M}$). Chem. synthesized 3-O-methyl-NDGA I ($R_3 = \text{Me}$, $R_4 = R_3' = R_4' = \text{H}$) showed identical anti-HIV activity ($\text{IC}_{50} 25 \mu\text{M}$) to the lignan isolated from Creosote Bush. Lignans with methylated catecholic hydroxyl groups can be produced in large quantities with low cost. At drug concns. below 30 μM , I ($R_3 = R_4 = R_3' = R_4' = \text{Me}$) was a stronger anti-HIV agent than mono- and dimethylated NDGAs.

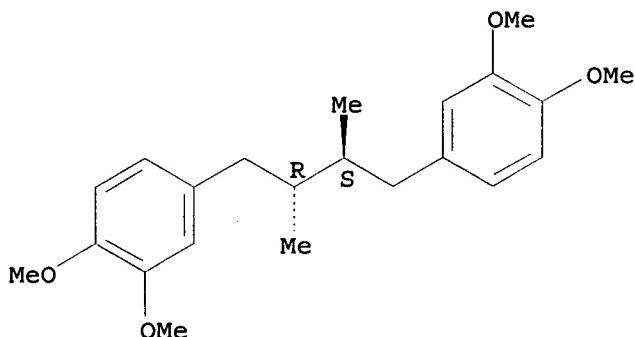
IT 24150-24-1P 66322-34-7P 71113-15-0P
171204-38-9P 171204-39-0P 171439-76-2P
212325-18-3P 212325-19-4P

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis, structure, and inhibition of Tat-regulated HIV transactivation of antiviral methylated nordihydroguaiaretic acids)

RN 24150-24-1 CAPLUS
CN Benzene, 1,1'-(2,3-dimethyl-1,4-butanediyl)bis[3,4-dimethoxy-, (R^*, S^*) - (9CI) (CA INDEX NAME)

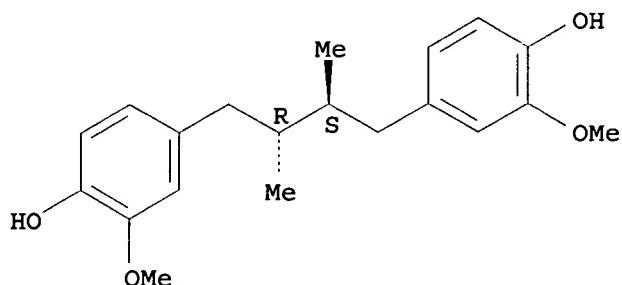
Relative stereochemistry.



RN 66322-34-7 CAPLUS
CN Phenol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis[2-methoxy-, (R^*, S^*) - (9CI) (CA INDEX NAME)

Relative stereochemistry.

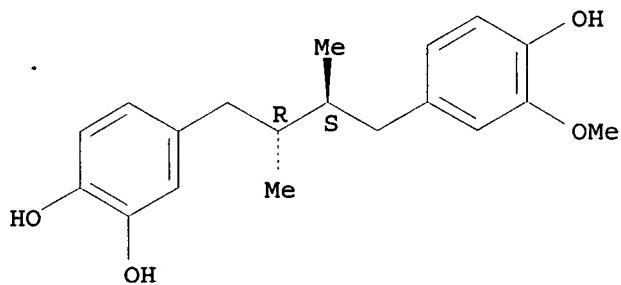
08/882499



RN 71113-15-0 CAPLUS

CN 1,2-Benzenediol, 4-[(2R,3S)-4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-, rel- (9CI) (CA INDEX NAME)

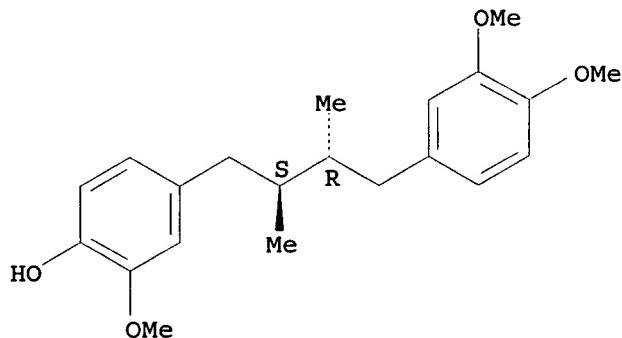
Relative stereochemistry.



RN 171204-38-9 CAPLUS

CN Phenol, 4-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



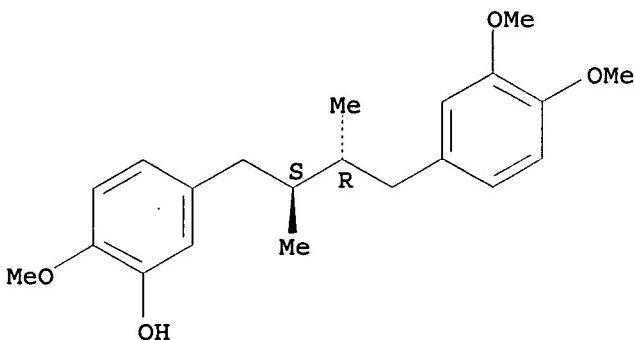
RN 171204-39-0 CAPLUS

Searcher : Shears 308-4994

08/882499

CN Phenol, 5-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

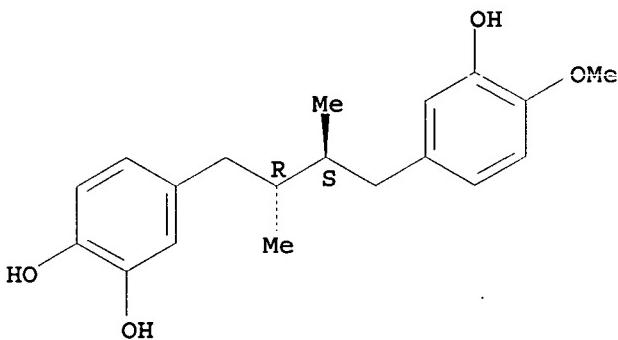
Relative stereochemistry.



RN 171439-76-2 CAPLUS

CN 1,2-Benzenediol, 4-[(2R,3S)-4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-, rel- (9CI) (CA INDEX NAME)

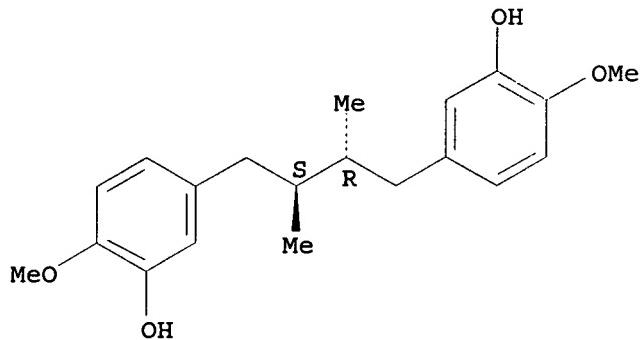
Relative stereochemistry.



RN 212325-18-3 CAPLUS

CN Phenol, 3,3'-(2R,3S)-2,3-dimethyl-1,4-butanediyl]bis[6-methoxy- (9CI) (CA INDEX NAME)

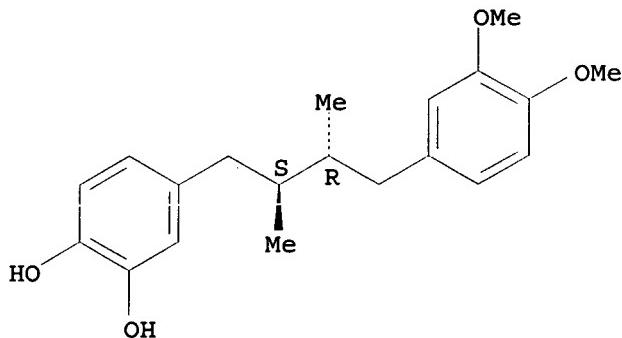
Relative stereochemistry.



RN 212325-19-4 CAPLUS

CN 1,2-Benzenediol, 4-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 27686-84-6, meso-Nordihydroguaiaretic acid

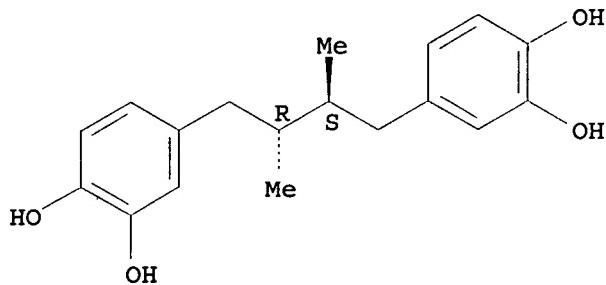
RL: PRP (Properties); RCT (Reactant)
 (synthesis, structure, and inhibition of Tat-regulated HIV
 transactivation of antiviral methylated
 nordihydroguaiaretic acids)

RN 27686-84-6 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis-, (R*,S*)-
 (9CI) (CA INDEX NAME)

Relative stereochemistry.

08/882499



IT 171204-43-6P

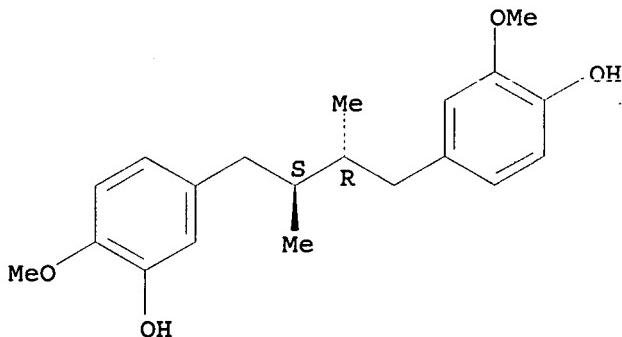
RL: PRP (Properties); SPN (Synthetic preparation); PREP
(Preparation)

(synthesis, structure, and inhibition of Tat-regulated HIV
transactivation of antiviral methylated
nordihydroguaiaretic acids)

RN 171204-43-6 CAPLUS

CN Phenol, 4-[(2R,3S)-4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-
2-methoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L12 ANSWER 6 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1998:341491 CAPLUS

DOCUMENT NUMBER: 129:12742

TITLE: Methods and compositions using thalidomide or
other angiogenesis-inhibitory compound and
anti-inflammatory agent for inhibition of
angiogenesis

INVENTOR(S): D'Amato, Robert J.

PATENT ASSIGNEE(S): Children's Medical Center, USA

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

Searcher : Shears 308-4994

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819649	A2	19980514	WO 97-US20116	19971104
WO 9819649	A3	19980625		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851973	A1	19980529	AU 98-51973	19971104
PRIORITY APPLN. INFO.:			US 96-28708	19961105
			US 97-963058	19971103
			WO 97-US20116	19971104

OTHER SOURCE(S): MARPAT 129:12742

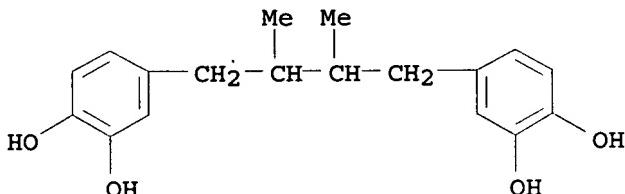
AB A group of compds. that effectively inhibit angiogenesis is provided. More specifically, thalidomide and various related compds., e.g. thalidomide precursors, analogs, metabolites and hydrolysis products, have been shown to inhibit angiogenesis and to treat disease states resulting from angiogenesis. Addnl., antiinflammatory drugs, such as steroids and NSAIDs can inhibit angiogenesis-dependent diseases either alone or in combination with thalidomide and related compds. Importantly, these compds. can be administered orally.

IT 500-38-9

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thalidomide or other angiogenesis-inhibitory compd. and anti-inflammatory agent for inhibition of angiogenesis)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 7 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:289269 CAPLUS
DOCUMENT NUMBER: 129:52663
TITLE: Retrograde trafficking of both Golgi complex and TGN markers to the ER induced by nordihydroguaiaretic acid and cyclofenil diphenol
AUTHOR(S): Drecktrah, Daniel; De Figueiredo, Paul; Mason, Roger M.; Brown, William J.
CORPORATE SOURCE: Section of Biochemistry, Molecular and Cell Biology, Cornell University, Ithaca, NY, 14853, USA
SOURCE: J. Cell Sci. (1998), 111(7), 951-965
CODEN: JNCSAI; ISSN: 0021-9533
PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies have shown that the Golgi stack and the trans-Golgi network (TGN) may play a role in capturing escaped resident endoplasmic reticulum (ER) proteins, and directing their retrograde transport back to that organelle. Whether this retrograde movement represents a highly specific or more generalized membrane trafficking pathway is unclear. To better understand both the retrograde and anterograde trafficking pathways of the secretory app., the in vivo effects of two structurally unrelated compds., the potent lipoxygenase inhibitor nordihydroguaiaretic acid (NDGA), and the non-steroidal estrogen cyclofenil diphenol (CFD), both of which are known to inhibit secretion, were examd. In the presence of these compds., transport of vesicular stomatitis virus G membrane glycoprotein from the ER to the Golgi complex, and from the TGN to the cell surface, was inhibited potently and rapidly. It was found that NDGA and CFD stimulated the rapid, but not concomitant, retrograde movement of both Golgi stack and TGN membrane proteins back to the ER until both organelles were morphol. absent from cells. Both NDGA- and CFD-stimulated TGN and Golgi retrograde membrane trafficking were inhibited by microtubule depolymg. agents and energy poisons. Removal of NDGA and CFD resulted in the complete, but not concomitant, reformation of both Golgi stacks and their closely assocd. TGN compartments. These studies suggest that NDGA and CFD unmask a generalized bulk recycling pathway to the ER for both Golgi and TGN membranes and, further, that NDGA and CFD are useful for investigating the mol. mechanisms that control the formation and maintenance of both the Golgi stack proper and the TGN.

IT 500-38-9, Nordihydroguaiaretic acid

RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(retrograde trafficking of both Golgi complex and TGN markers to

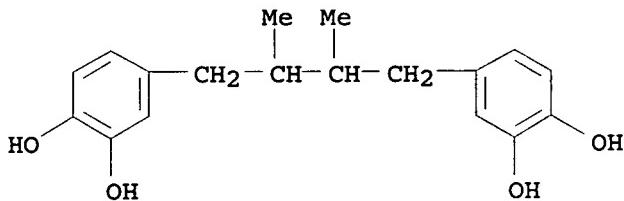
Searcher : Shears 308-4994

08/882499

the endoplasmic reticulum induced by nordihydroguaiaretic acid
and cyclofenil diphenol)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
INDEX NAME)



L12 ANSWER 8 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1998:239082 CAPLUS

DOCUMENT NUMBER: 128:275069

TITLE: Nontoxic therapeutic extract of *Larrea tridentata*

INVENTOR(S): Sinnott, Robert A.; Clark, Dennis W.; De Boer, Kenneth Frank

PATENT ASSIGNEE(S): LarreaCorp, Ltd., USA; Sinnott, Robert A.; Clark, Dennis W.; De Boer, Kenneth Frank

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815184	A1	19980416	WO 97-US18103	19971007
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW			
US 5837252	A	19981117	US 96-726686	19961007
AU 9748956	A1	19980505	AU 97-48956	19971007
WO 9917609	A1	19990415	WO 98-US19817	19980914
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

Searcher : Shears 308-4994

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 96-726686	19961007
	WO 97-US18103	19971007
	US 97-64674	19971020
	US 97-64802	19971020
	US 97-64803	19971020
	US 97-64804	19971020
	US 97-64805	19971020

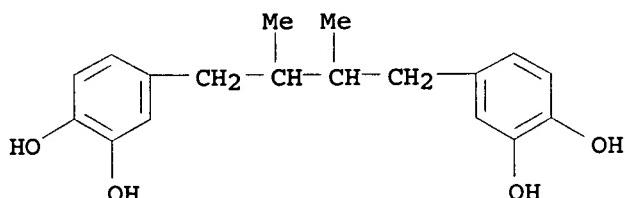
AB A nontoxic, therapeutic agent having pharmacol. activity comprising concd. ext. of *Larrea tridentata* and a reducing agent, such as ascorbic acid, an ascorbic acid ester, an ascorbic acid salt, butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulfide, hypophosphorous acid, monothioglycerol, potassium bisulfite, Pr gallate, sodium bisulfite, sodium hydrosulfite, sodium thiosulfate, sulfur dioxide, sulfurous acid, a tocopherol, or vitamin E. The active principle is nordihydroguaiaretic acid (NDGA). The plant material is extd. using an org. solvent, preferably acetone, and is then satd. with one of the listed reducing agents to reduce the toxic NDGA quinone, which naturally occurs in the plant material, to NDGA itself. Addnl. amts. of reducing agent may be added to the ext. to inhibit the natural oxidn. of the NDGA into the toxic NDGA quinone *in vivo*, or during processing or storage. The resulting ext. is useful in the treatment of viral diseases caused by viruses from the *Herpesviridae* family or viruses which require the Sp1 class of proteins to initiate viral replications. The resulting compd. can also be used as an anti-inflammatory agent when the inflammatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize NDGA as a therapeutic agent or a food additive.

IT 500-38-9P, Nordihydroguaiaretic acid

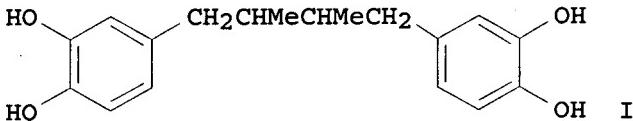
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(active principle in therapeutic ext. of *Larrea tridentata*)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 9 OF 29 CAPLUS COPYRIGHT 1999 ACS
 ACCESSION NUMBER: 1998:163109 CAPLUS
 DOCUMENT NUMBER: 128:280435
 TITLE: Purification of anti-HIV lignans from *Larrea tridentata* by pH-zone-refining countercurrent chromatography
 AUTHOR(S): Ma, Y.; Qi, L.; Gnabre, J. N.; Huang, R. C. C.; Chou, F. E.; Ito, Y.
 CORPORATE SOURCE: Laboratory of Biomedical Chemistry, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, 20892-1676, USA
 SOURCE: *J. Liq. Chromatogr. Relat. Technol.* (1998), 21(1 & 2), 171-181
 CODEN: JLCTFC; ISSN: 1082-6076
 PUBLISHER: Marcel Dekker, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Anti-HIV lignans were purified from ext. of *Larrea tridentata* by high-speed countercurrent chromatog. (CCC) using pH-zone-refining CCC. When a column filled with Me t-Bu ether, contg. trifluoroacetic acid at 25 mM, was eluted with aq. NaOH, 10 to 20 g of the crude ext. was sepd. into NDGA (I) and its monomethyl esters rectangular peaks assocd. with their specific pH (pH zones). The method was also successfully applied to synthetic lignans, resulting in resln. of NDGA and its mono and di-Me esters.

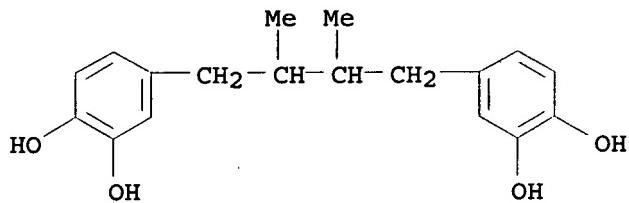
IT 500-38-9P, NDGA 54473-24-4P 178557-46-5P

205758-62-9P

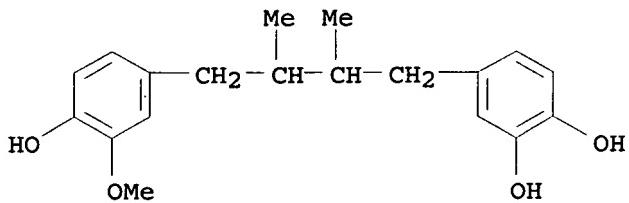
RL: PUR (Purification or recovery); PREP (Preparation)
 (purifn. of anti-HIV lignans from *Larrea tridentata* by pH-zone-refining countercurrent chromatog.)

RN 500-38-9 CAPLUS

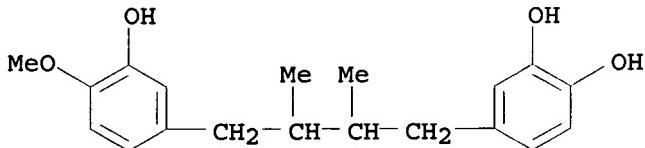
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



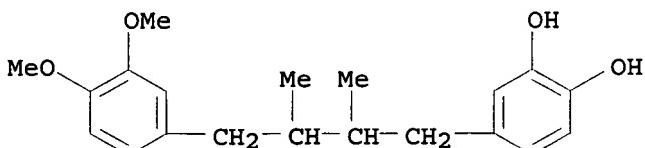
RN 54473-24-4 CAPLUS

CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-
(9CI) (CA INDEX NAME)

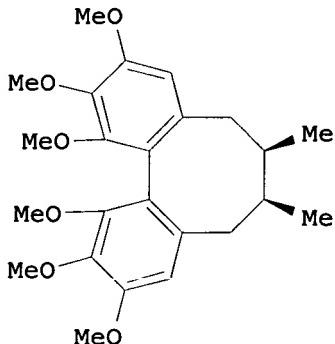
RN 178557-46-5 CAPLUS

CN 1,2-Benzenediol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-
(9CI) (CA INDEX NAME)

RN 205758-62-9 CAPLUS

CN 1,2-Benzenediol, 4-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-
(9CI) (CA INDEX NAME)

DOCUMENT NUMBER: 127:190585
 TITLE: A new synthesis method for (.-+.)-
 deoxyschizandrin
 AUTHOR(S): Wu, Anxin; Zhao, Yurui; Qin, Binchang; Chen,
 Ning; Pan, Xinfu
 CORPORATE SOURCE: State Key Laboratory of Applied Organic
 Chemistry, Department of Chemistry, Lanzhou
 University, Lanzhou, 730000, Peop. Rep. China
 SOURCE: Chin. Sci. Bull. (1997), 42(12), 995-998
 CODEN: CSBUEF; ISSN: 1001-6538
 PUBLISHER: Science Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



I

AB Deoxyschizandrin (I) isolated from *Schizandra chinensis* exhibits antihepatitis virus activity. Interest in the synthesis of I comes from its bioactivity. A new very efficient route to the synthesis of (.-+.)-deoxyschizandrin via gallic acid in 10 steps with the overall yield of 12% and using the I₂/NaOEt oxidative coupling reaction as a key step is described.

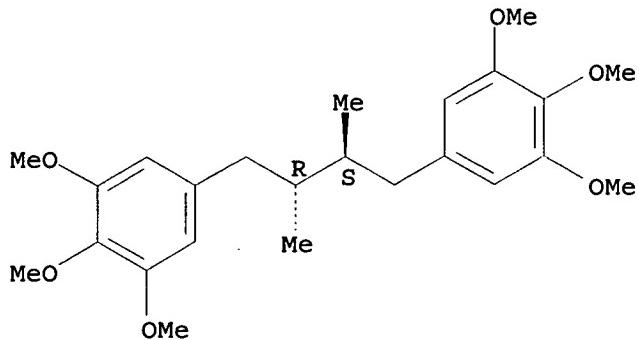
IT 72730-20-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (new method for the prepn. of (.-+.)-deoxyschizandrin)

RN 72730-20-2 CAPLUS

CN Benzene, 1,1'-(2,3-dimethyl-1,4-butanediyl)bis[3,4,5-trimethoxy-, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L12 ANSWER 11 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1997:332397 CAPLUS

DOCUMENT NUMBER: 126:301796

TITLE: Use of 2-mercaptoproethanolamine (2-MEA) and related aminothiol compounds and copper(II)-3,5 diisopropyl salicylates and related compounds in the prevention and treatment of AIDS, cancer, autoimmune disease, microbiological infections, and other diseases

INVENTOR(S): Chachoua, Samir

PATENT ASSIGNEE(S): Chachoua, Samir, Mex.

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9711666	A2	19970403	WO 96-IB1059	19960925
WO 9711666	A3	19970619		
W:	AL, AM, AU, BB, BG, BR, CA, CN, CU, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2233015	AA	19970403	CA 96-2233015	19960925
CA 2233445	AA	19970403	CA 96-2233445	19960925
AU 9669990	A1	19970417	AU 96-69990	19960925
EP 858327	A2	19980819	EP 96-931214	19960925
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

Searcher : Shears 308-4994

08/882499

PRIORITY APPLN. INFO.: US 95-4281 19950925
WO 96-IB1059 19960925

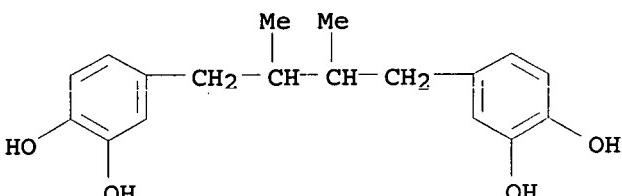
AB New therapeutic compns. and applications of 2-MEA and related aminothiols and copper(II)-3,5-diisopropyl salicylates, solely or in combination with other factors, agents, or processes that are phys., chem. and/or biol.-based, are disclosed. These include precursors, intermediates, end products, catalysts, promoters and/or any factors, agents, or processes involved directly or indirectly from initial application of the compns. to the final result. The methods and compns. of the invention are useful for the treatment of AIDS, cancer, autoimmune disease, and microbiol. infections, as well as other diseases in which immunol. dysfunction and/or free radical formation function as part of the disease mechanism.

IT 500-38-9

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mercaptoethanolamine, related aminothiols, copper diisopropyl salicylate, and related compds., alone or in combination, for prevention and treatment of disease)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 12 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1997:142788 CAPLUS
DOCUMENT NUMBER: 126:224234
TITLE: Activation of the NF-KB transcription factor in a T-lymphocytic cell line by hypochlorous acid
AUTHOR(S): Schoonbroodt, Sonia; Legrand-Poels, Sylvie; Best-Belpomme, Martin; Piette, Jacques
CORPORATE SOURCE: Laboratory of Virology, institute of Pathology B23, University of Liege, Liege, B-4000, Belg.
SOURCE: Biochem. J. (1997), 321(3), 777-785
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reactive oxygen species (ROS) such as hydrogen peroxide serve as second messengers in the induction of the transcription factor
Searcher : Shears 308-4994

NF-.kappa.B, and hence in the activation and replication of human immunodeficiency virus type 1 (HIV-1) in human cells.

During inflammatory reactions, many oxidative species are produced, one of which is hypochlorous acid (HOCl), which is responsible for the microbicidal effects of activated human polymorphonuclear leukocytes. Treatment of a T-lymphocytic cell line with micromolar concns. of HOCl promoted the appearance of transcription factor NF-.kappa.B (the heterodimer p50/p65) in the nucleus of the cells, even in the absence of de novo protein synthesis. Western blot anal. of the NF-.kappa.B inhibitory subunits (I.kappa.B) demonstrated that both I.kappa.B-.alpha. proteolysis and p105 processing were induced by the treatment. NF-.kappa.B activation was very effective when cells were subjected to hyperthermia before being treated with HOCl. Various antioxidants, such as pyrrolidine dithiocarbamate, p-bromophenacyl-bromide and nordihydroguaiaretic acid could strongly reduce NF-.kappa.B translocation, demonstrating the importance of oxidative species in the transduction mechanism. Moreover, ACH-2 cells treated with HOCl or H2O2 released tumor necrosis factor-.alpha. (TNF-.alpha.) in the supernatants. The importance of TNF-.alpha. release in NF-.kappa.B induction by HOCl or H2O2 was demonstrated by the fact that: (1) the nuclear appearance of NF-.kappa.B was promoted in untreated cells; and (2) synergism between TNF-.alpha. and HOCl was detected. Collectively, these results suggest that HOCl should be considered as an oxidative species capable of inducing NF-.kappa.B in a T-lymphocytic cell line through a transduction mechanism involving ROS, and having a long-distance effect through subsequent TNF-.alpha. release.

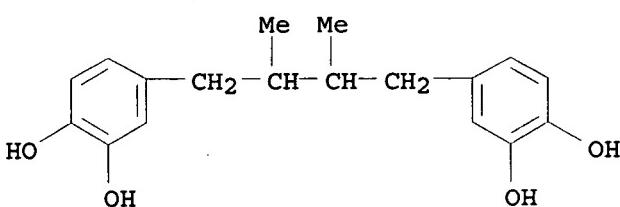
IT 500-38-9, Nordihydroguaiaretic acid

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(activation of the NF-KB transcription factor in a T-lymphocytic cell line by hypochlorous acid response to)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 13 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1996:425306 CAPLUS

DOCUMENT NUMBER: 125:76343

Searcher : Shears 308-4994

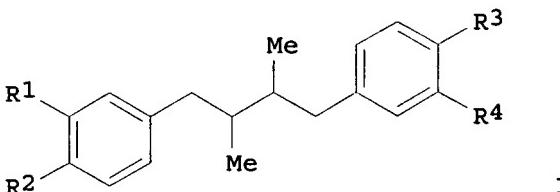
08/882499

TITLE: Nordihydroguaiaretic acid derivatives for the suppression of HIV Tat transactivation
INVENTOR(S): Huang, Ru Chih; Gnabbe, John N.
PATENT ASSIGNEE(S): Johns-Hopkins University, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610549	A1	19960411	WO 95-US11779	19950922
W: AU, CA, CN, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2200991	AA	19960411	CA 95-2200991	19950922
AU 9536339	A1	19960426	AU 95-36339	19950922
AU 700481	B2	19990107		
EP 783474	A1	19970716	EP 95-933830	19950922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1162301	A	19971015	CN 95-196035	19950922
JP 10509421	T2	19980914	JP 95-511844	19950922
US 5663209	A	19970902	US 96-627588	19960404
PRIORITY APPLN. INFO.:			US 94-316341	19940930
			WO 95-US11779	19950922

OTHER SOURCE(S): MARPAT 125:76343

GI



AB The invention reveals the isolation, purifn. and characterization from the creosote bush Larrea tridentata of compds. I [R1-R4 = OH, OMe, CH₃C(O)O, provided that R1-R4 are not each OH simultaneously]. Each compd. is a deriv. of 1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane (nordihydroguaiaretic acid, NDGA). In addn., NDGA and each deriv. can be used in a method to suppress Tat transactivation of a lentivirus, including the HIV virus, in a cell by administering NDGA or a deriv. of NDGA to the cell.

Searcher : Shears 308-4994

08/882499

Fractionation of NDGA derivs. from Larrea tridentata is described.
Inhibition of transactivation of HIV promoter activity by NDGA and
4-O-methyl-NDGA was detd.

IT 500-38-9DP, Nordihydroguaiaretic acid, derivs.

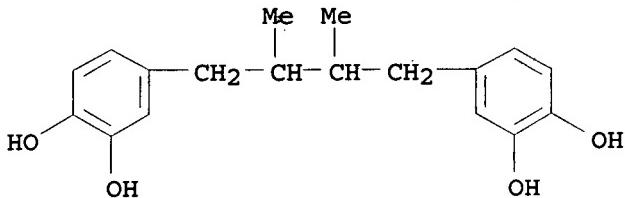
500-38-9P, Nordihydroguaiaretic acid 178557-46-5P

RL: BAC (Biological activity or effector, except adverse); PUR
(Purification or recovery); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)

(nordihydroguaiaretic acid derivs. from Larrea tridentata for
suppression of Tat transactivation of HIV or other lentivirus)

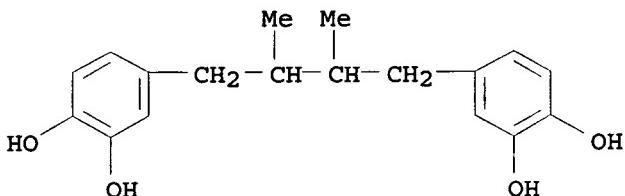
RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
INDEX NAME)



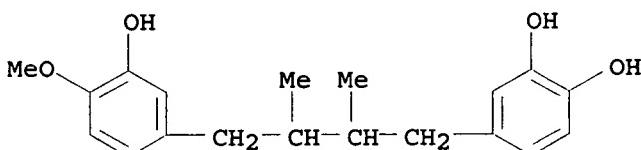
RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
INDEX NAME)



RN 178557-46-5 CAPLUS

CN 1,2-Benzenediol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-
(9CI) (CA INDEX NAME)



IT 54473-24-4P 178557-47-6P 178557-48-7P

Searcher : Shears 308-4994

08/882499

178557-49-8P 178557-50-1P 178557-51-2P

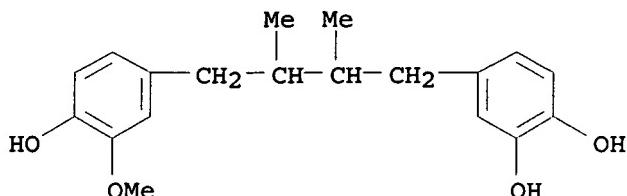
178557-52-3P 178557-53-4P

RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); USES (Uses)

(nordihydroguaiaretic acid derivs. from Larrea tridentata for
suppression of Tat transactivation of HIV or other lentivirus)

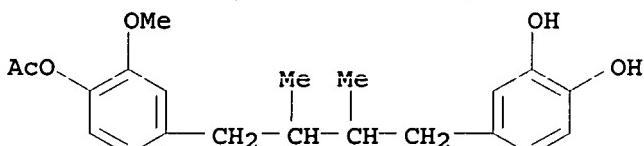
RN 54473-24-4 CAPLUS

CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-
(9CI) (CA INDEX NAME)



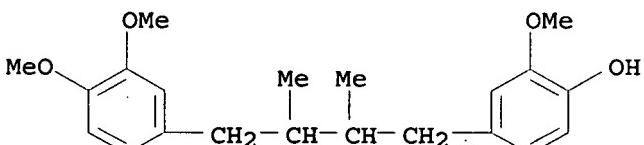
RN 178557-47-6 CAPLUS

CN 1,2-Benzenediol, 4-[4-[4-(acetoxy)-3-methoxyphenyl]-2,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



RN 178557-48-7 CAPLUS

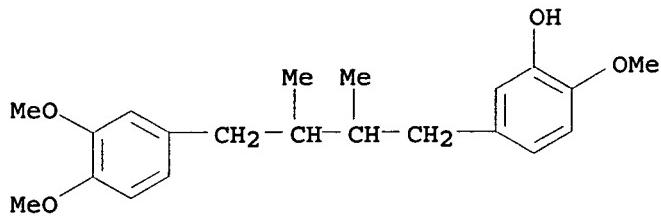
CN Phenol, 4-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-
(9CI) (CA INDEX NAME)



RN 178557-49-8 CAPLUS

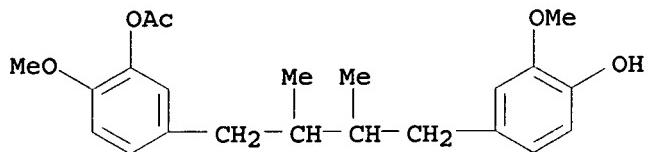
CN Phenol, 5-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-
(9CI) (CA INDEX NAME)

Searcher : Shears 308-4994



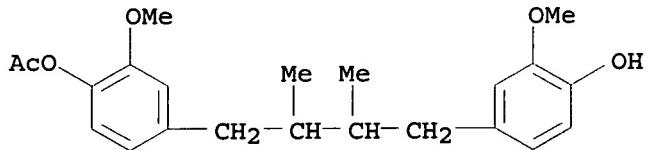
RN 178557-50-1 CAPLUS

CN Phenol, 4-[4-[3-(acetyloxy)-4-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy- (9CI) (CA INDEX NAME)



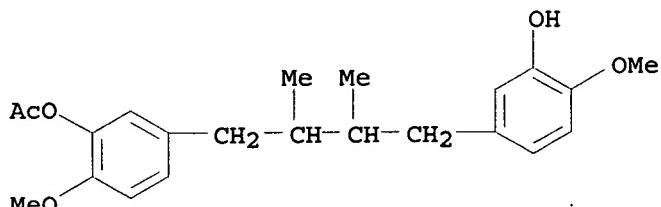
RN 178557-51-2 CAPLUS

CN Phenol, 4-[4-[4-(acetyloxy)-3-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 178557-52-3 CAPLUS

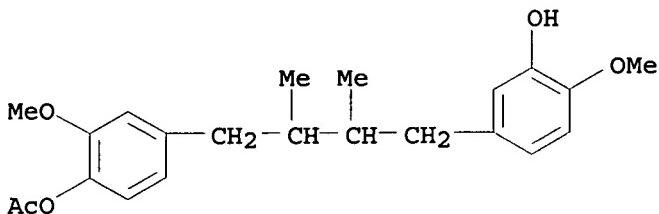
CN Phenol, 5-[4-[3-(acetyloxy)-4-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 178557-53-4 CAPLUS

Searcher : Shears 308-4994

CN Phenol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, 1-acetate (9CI) (CA INDEX NAME)



L12 ANSWER 14 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1996:371202 CAPLUS
 DOCUMENT NUMBER: 125:54332
 TITLE: Inhibition of vesicle-mediated protein transport by nordihydroguaiaretic acid
 AUTHOR(S): Tagaya, Mitsuo; Henomatsu, Nobuhiro; Yoshimori, Tamotsu; Yamamoto, Akitsugu; Tashiro, Yutaka; Mizushima, Shoji
 CORPORATE SOURCE: Sch. Life Sci., Tokyo Univ. Pharm. Life Sci., Hachioji, 192-03, Japan
 SOURCE: J. Biochem. (Tokyo) (1996), 119(5), 863-869
 CODEN: JOBIAO; ISSN: 0021-924X
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Nordihydroguaiaretic acid (NDGA), a phospholipase A2 inhibitor, blocks intra-Golgi protein transport in a cell-free system and prolactin secretion from HG2 cells [Tagaya, M., Henomatsu, N., Yoshimiri, T., Yamamoto, A., Tashiro, Y., and Fukui, T. (1993) FEBS Lett. 324, 201-204]. To det. which intracellular secretory pathway(s) is inhibited by NDGA, we investigated its effect on the transport of the vesicular stomatitis virus-encoded glycoprotein in BHK-21 cells. NDGA blocked protein transport from the endoplasmic reticulum to the Golgi app., and from the trans-Golgi network to the plasma membrane. In addn., it retarded the brefeldin A-induced retrograde transport of mannosidase II to the endoplasmic reticulum. Although NDGA had an inhibitory effect on protein synthesis, it induced the expression of BiP, a chaperone located in the endoplasmic reticulum. The induction of BiP may be a consequence of the inhibition of protein transport by NDGA.

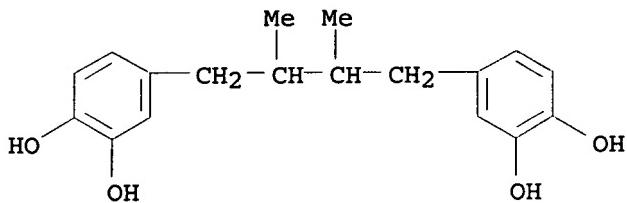
IT 500-38-9, Nordihydroguaiaretic acid
 RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (inhibition of vesicle-mediated protein transport by nordihydroguaiaretic acid, a phospholipase A2 inhibitor)

RN 500-38-9 CAPLUS

Searcher : Shears 308-4994

08/882499

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
INDEX NAME)



L12 ANSWER 15 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1996:309295 CAPLUS

DOCUMENT NUMBER: 125:1316

TITLE: Effects of cellular aging on the induction of c-fos by antioxidant treatments

AUTHOR(S): Keogh, Bart P.; Tresini, Maria; Cristofalo, Vincent J.; Allen, R. G.

CORPORATE SOURCE: Center Gerontological Research, Medical College Pennsylvania, Philadelphia, PA, 19129, USA

SOURCE: Mech. Ageing Dev. (1996), 86(3), 151-160

CODEN: MAGDA3; ISSN: 0047-6374

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The proto-oncogene c-fos (the cellular homolog of v-fos, Finkel-Biskis-Jenkins (FBJ) murine osteogenic sarcoma virus) encodes a major component of the activator protein-1 (AP-1) transcription factor. Serum stimulation as well as oxidizing treatments induce transitory increases in c-fos mRNA abundance. The induction of c-fos by serum stimulation is also known to decline during proliferative senescence. In this study, we examd. the effects of two classes of antioxidants on the induction of c-fos in early and late passage human fetal lung fibroblasts (WI-38).

N-acetyl cysteine (NAC) induces c-fos transcription in both early and late passage cells, while nordihydroguaiaretic acid (NGA) induced c-fos transcription in early passage cells but fails to stimulate it in late passage cells. Since we had previously obsd. an age-related decline in protein kinase C (PKC) translocation from the cytosol to the membrane, following its activation, and because PKC activation appears to be involved in the NGA induction of c-fos we examd. the relative protein abundances of several PKC isoforms in early and late passage cells. Addnl., we examd. the protein abundance of several members of the MAP kinase pathway which could play a role in c-fos induction by the PKC-dependent pathway. We were unable to detect PKC-.beta. in early or late passage cells. Late passage cells contained a slightly greater abundance of PKC .alpha., .gamma. and .epsilon. than cells at an early passage. No

Searcher : Shears 308-4994

08/882499

other differences in PKC isoforms or in members of the MAP kinase family were obsd. in early or late passage cells. These results clearly demonstrate that at least some pathways leading to c-fos induction remain intact in late passage cells.

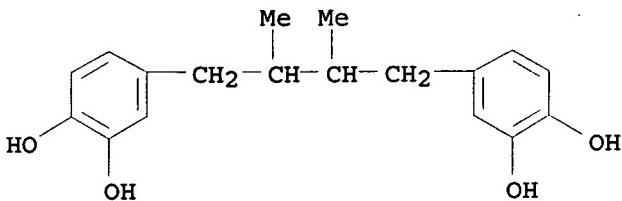
IT 500-38-9, Nordihydroguaiaretic acid

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(effects of cellular aging on induction of c-fos by antioxidant treatments)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 16 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1996:135789 CAPLUS

DOCUMENT NUMBER: 124:167496

TITLE: Enhancement of introduction of foreign matter into higher eukaryotic cells by co-introduction of anti-apoptosis or anti-inflammatory substances

INVENTOR(S): Cotten, Matthew; Baker, Adam; Chiocca, Susanna

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany

SOURCE: PCT Int. Appl., 99 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9533062	A2	19951207	WO 95-EP1989	19950526
W:	AU, BR, CA, CN, JP, KR, MX, PL, RU, US			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
DE 4418825	A1	19951207	DE 94-4418825	19940530
DE 4442587	A1	19960801	DE 94-4442587	19941130
AU 9526160	A1	19951221	AU 95-26160	19950526
EP 767840	A2	19970416	EP 95-920887	19950526

Searcher : Shears 308-4994

08/882499

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,
PT, SE

JP 10500578 T2 19980120 JP 95-500282 19950526
DE 94-4418825 19940530
DE 94-4442587 19941130
WO 95-EP1989 19950526

PRIORITY APPLN. INFO.:

AB The toxicity problems arising when foreign matter is introduced into higher eukaryotic cells, esp. with transfection with DNA, are obviated by expression in the cell of gene products that block the apoptosis induced by the transfection process and/or by treating the cells with anti-inflammatory substances. Preferred anti-apoptosis genes are Bcl-2, adenovirus E1B 19K or an anti-apoptotic gene of the CELO avian adenovirus. The preferred anti-inflammatory substance is adenovirus VA1, which is introduced into the cell in the form of VA1 DNA. These measures help to achieve a long-lasting gene expression. The anti-apoptotic gene of CELO virus was cloned and sequenced. The enhancement by the above genes of mammalian cell transfection using transferrin (or streptavidin)-polylysine conjugate/adenovirus transfection complexes was demonstrated. The synergistic effect of anti-inflammatory compds. such as glucocorticoids, ibuprofen, etc. was also shown.

IT 500-38-9, NDGA

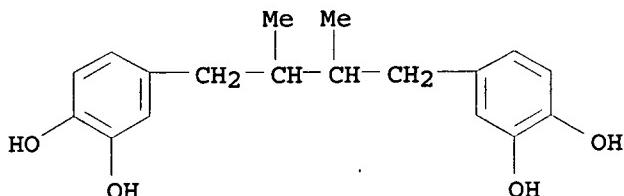
RL: BUU (Biological use, unclassified); BIOL (Biological study);

USES (Uses)

(enhancement of introduction of foreign matter into higher eukaryotic cells by co-introduction of anti-apoptosis or anti-inflammatory substances)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 17 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1996:58761 CAPLUS

DOCUMENT NUMBER: 124:211685

TITLE: Isolation of anti-HIV-1 lignans from Larrea tridentata by counter-current chromatography

AUTHOR(S): Gnabre, John Noel; Ito, Yoichiro; Ma, Ying;
Huang, Ru Chih

CORPORATE SOURCE: Department of Biology, The Johns Hopkins
Searcher : Shears 308-4994

08/882499

University, 144 Mudd Hall, 3400 N. Charles
Street, Baltimore, MD, 21218-2685, USA

SOURCE: J. Chromatogr., A (1996), 719(2), 353-64
CODEN: JCRAEY; ISSN: 0021-9673

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several lignans, mostly new, were isolated from *Larrea tridentata* by assay-guided counter-current chromatog. (CCC). Using the secreted alk. phosphatase bioassay of HIV Tat transactivation and the 2-phase hexane-Et acetate-methanol-water solvent system, 2 major components (Gr and Lo) were identified as anti-HIV active principles. The chem. structures of the constituents of Gr (G1-G4) and Lo (L1-L4) were detd. by GC-MS and NMR. After optimization of isolation conditions, a large-scale isolation with the chloroform-methanol-water system yielded 5 constituents (FB1-FB5). The most predominant anti-HIV compd. FB2 (denoted Malachi 4:5-6 or mal.4), which occurs in 0.23% yield, was sepd. from its FB1 isomer (0.13% yield). Compd. FB4 and 2 tricyclic lignans (FB3 and FB5) were also isolated in a substantial amt. for further testing of their anti-HIV activities. These compds. may represent a new class of anti-HIV agents with important clin. relevance.

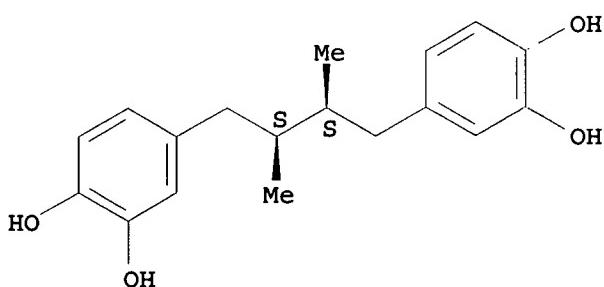
IT 119584-39-3 174155-42-1 174155-43-2
174155-45-4 174291-51-1 174291-52-2
174291-53-3 174291-54-4 174291-55-5
174291-56-6

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(isolation of anti-HIV-1 lignans from *Larrea tridentata* by counter-current chromatog.)

RN 119584-39-3 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis-,
[S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

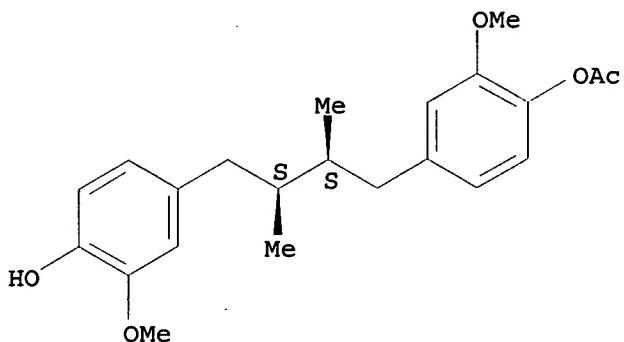


RN 174155-42-1 CAPLUS

CN Phenol, 4-[4-[4-(acetoxy)-3-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Searcher : Shears 308-4994

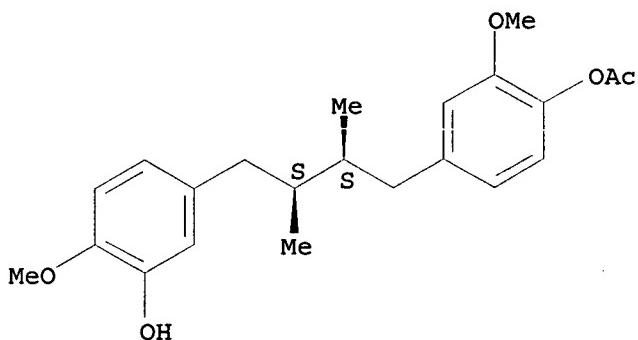
Absolute stereochemistry.



RN 174155-43-2 CAPLUS

CN Phenol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, 1-acetate, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

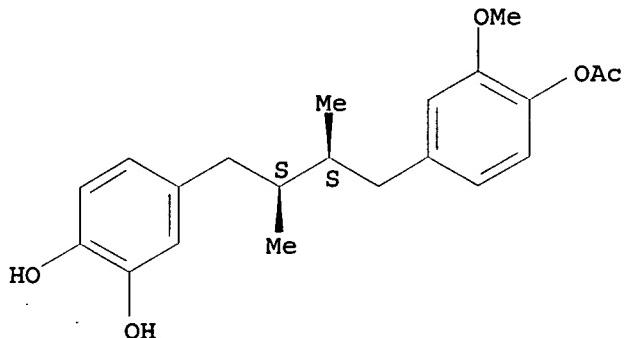


RN 174155-45-4 CAPLUS

CN 1,2-Benzenediol, 4-[4-[4-(acetoxy)-3-methoxyphenyl]-2,3-dimethylbutyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

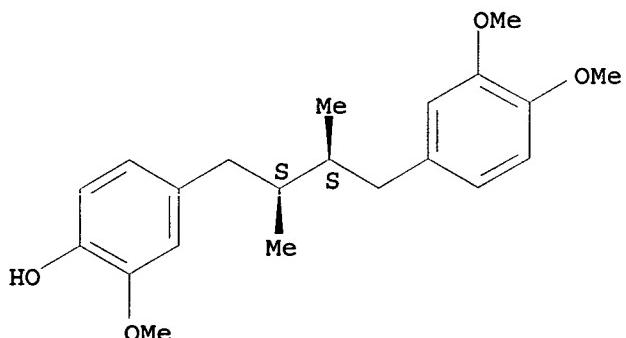
08/882499



RN 174291-51-1 CAPLUS

CN Phenol, 4-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-,
[S-(R*,R*)] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

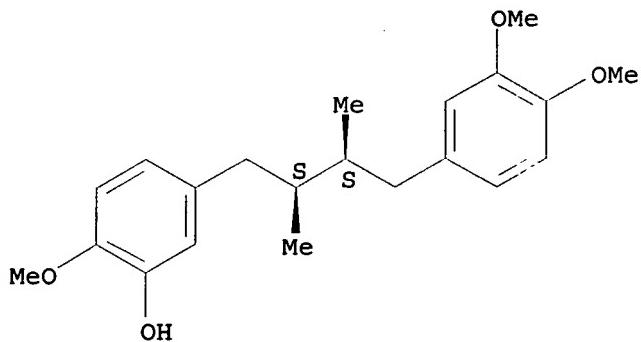


RN 174291-52-2 CAPLUS

CN Phenol, 5-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-,
[S-(R*,R*)] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

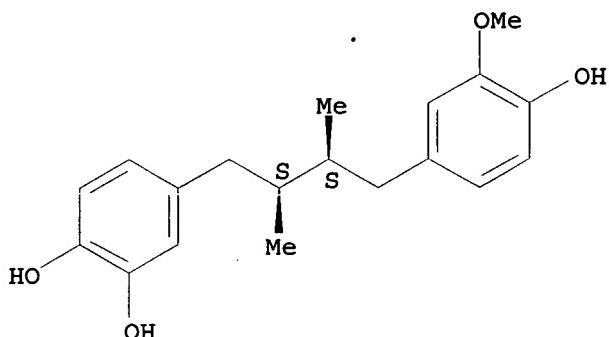
08/882499



RN 174291-53-3 CAPLUS

CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

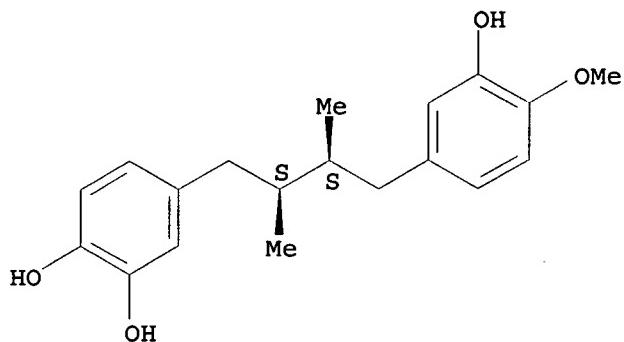
Absolute stereochemistry.



RN 174291-54-4 CAPLUS

CN 1,2-Benzenediol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

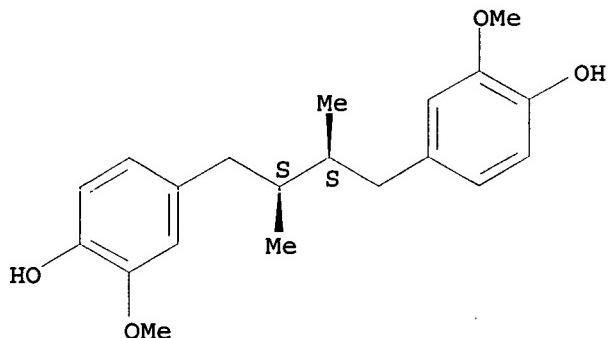
Absolute stereochemistry.



RN 174291-55-5 CAPLUS

CN Phenol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis[2-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

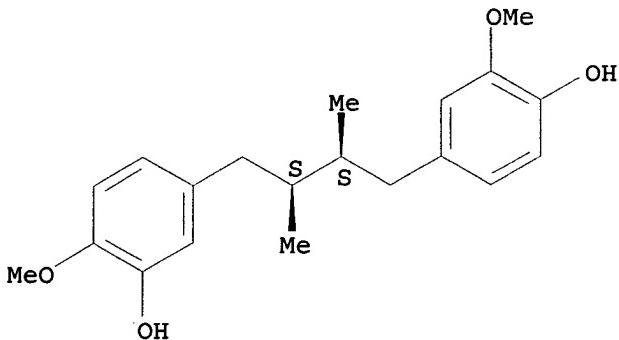
Absolute stereochemistry.



RN 174291-56-6 CAPLUS

CN Phenol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 18 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1995:962655 CAPLUS
 DOCUMENT NUMBER: 124:105660
 TITLE: Inhibition of human immunodeficiency virus type 1 transcription and replication by DNA sequence-selective plant lignans
 AUTHOR(S): Gnabre, John N.; Brady, John N.; Clanton, David J.; Ito, Yoichiro; Dittmer, Juergen; Bates, Robert B.; Huang, Ru Chih C.
 CORPORATE SOURCE: Dep. Biol., Johns Hopkins Univ., Baltimore, MD, 21218, USA
 SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1995), 92(24), 11239-43
 CODEN: PNASA6; ISSN: 0027-8424
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB A plant lignan, 3'-O-Me nordihydroguaiaretic acid (3'-O-Me NDGA, denoted Malachi 4:5-6 or Mal.4; mol. wt. 316), was isolated from Larrea tridentata and found to be able to inhibit human immunodeficiency virus (HIV) Tat-regulated transactivation in vivo, induce protection of lymphoblastoid CEM-SS cells from HIV (strain IIIB) killing, and suppress the replication of five HIV-1 strains (WM, MN, VS, JR-CSF, and IIIB) in mitogen-stimulated peripheral blood mononuclear cells, all in a dose-dependent manner. Mal.4 inhibits both basal transcription and Tat-regulated transactivation in vitro. The target of Mal.4 has been localized to nucleotides -87 to -40 of the HIV long terminal repeat. Mal.4 directly and specifically interferes with the binding of Sp1 to Sp1 sites in the HIV long terminal repeat. By inhibiting proviral expression, Mal.4 may be able to interrupt the life cycles of both wild-type and reverse transcriptase or protease mutant viruses in HIV-infected patients.

IT 500-38-9, NDGA 171204-41-4

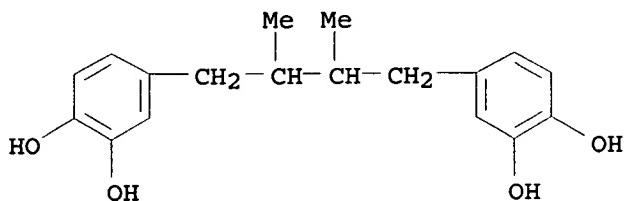
Searcher : Shears 308-4994

08/882499

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of human immunodeficiency virus type 1 transcription and replication by DNA sequence-selective plant lignans)

RN 500-38-9 CAPLUS

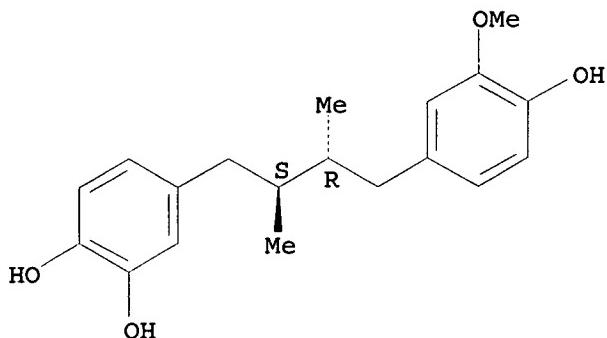
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



RN 171204-41-4 CAPLUS

CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-, (R*,S*)-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



L12 ANSWER 19 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1995:927912 CAPLUS
DOCUMENT NUMBER: 124:25594
TITLE: Characterization of anti-HIV lignans from Larrea tridentata.
AUTHOR(S): Gnabre, John; Huang, Ru Chih C.; Bates, Robert B.; Burns, Jennifer J.; Caldera, Sriyani; Malcomson, Mark E.; McClure, Kelly J.
CORPORATE SOURCE: Dep. Biology, Johns Hopkins Univ., Baltimore, MD, 21218-2685, USA
SOURCE: Tetrahedron (1995), 51(45), 12203-10
Searcher : Shears 308-4994

CODEN: TETRAB; ISSN: 0040-4020

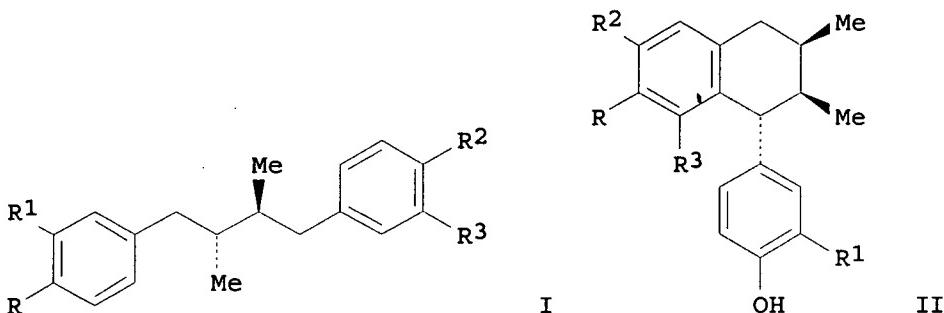
DOCUMENT TYPE:

Journal

LANGUAGE:

English

GI



AB Fractions from *L. tridentata* with anti-HIV-1 activity (specifically, inhibition of HIV Tat transactivation) were analyzed by GC/MS and NMR and found to contain lignans I ($R=OH, OMe, OAc; R1, R2=OH, OMe; R3=H, R$) and II ($R=OH, OMe; R1=H, OH, OMe; R2, R3=H, OH$). Assay-guided purifn. by countercurrent chromatog. established I ($R=R2=R3=OH, R1=OMe$) to be esp. active.

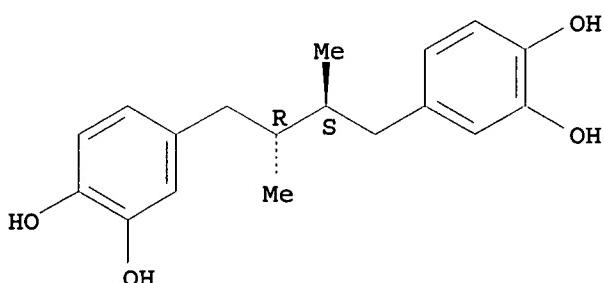
IT 27686-84-6P 66322-34-7P 171204-38-9P
 171204-39-0P 171204-41-4P 171204-42-5P
 171204-43-6P 171439-75-1P 171439-77-3P
 171439-78-4P

RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (anti-HIV lignan from *Larrea tridentata*)

RN 27686-84-6 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis-, (R^*, S^*) -
 (9CI) (CA INDEX NAME)

Relative stereochemistry.

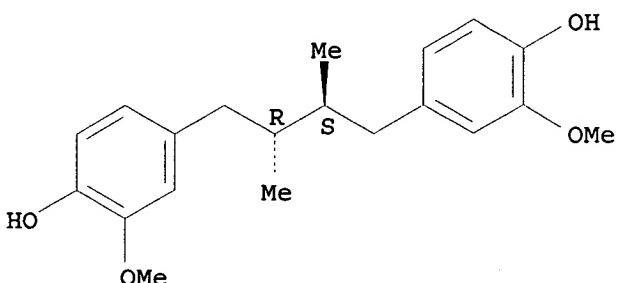


08/882499

RN 66322-34-7 CAPLUS

CN Phenol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis[2-methoxy-, (R*,S*)-
(9CI) (CA INDEX NAME)

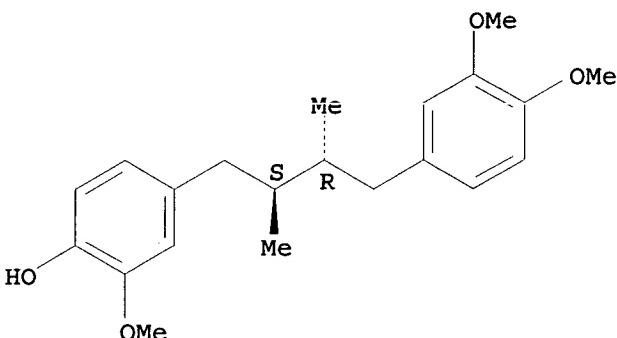
Relative stereochemistry.



RN 171204-38-9 CAPLUS

CN Phenol, 4-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-
methoxy-, rel- (9CI) (CA INDEX NAME)

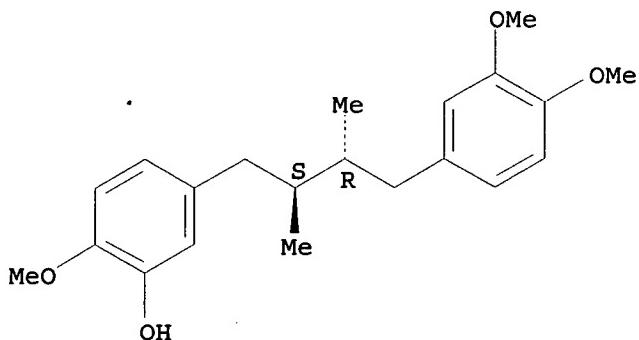
Relative stereochemistry.



RN 171204-39-0 CAPLUS

CN Phenol, 5-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-
methoxy-, rel- (9CI) (CA INDEX NAME)

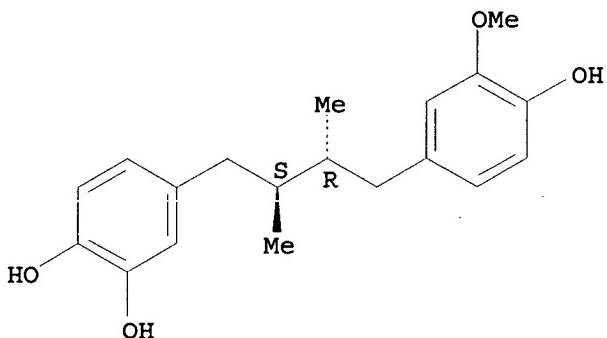
Relative stereochemistry.



RN 171204-41-4 CAPLUS

CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-,
(R*,S*)-(+)-(9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.

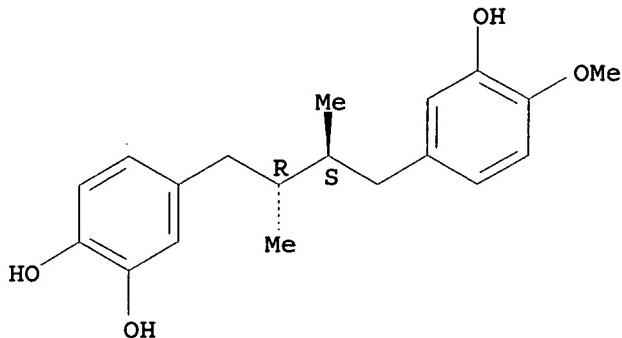


RN 171204-42-5 CAPLUS

CN 1,2-Benzenediol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-,
(R*,S*)-(+)-(9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.

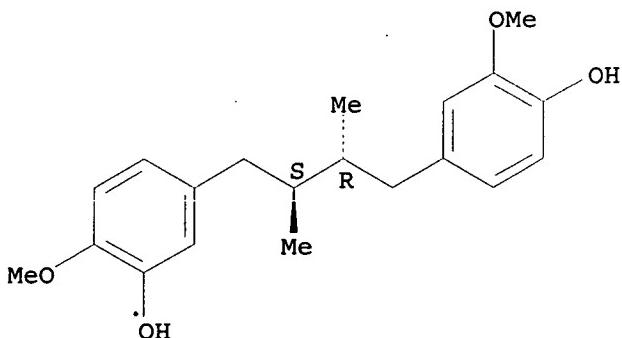
08/882499



RN 171204-43-6 CAPLUS

CN Phenol, 4-[(2R,3S)-4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171439-75-1 CAPLUS

CN Phenol, 4-[4-[3(or 4)-(acetoxy)-4(or 3)-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy-, (R*,S*)- (9CI) (CA INDEX NAME)

CM 1

CRN 71113-15-0

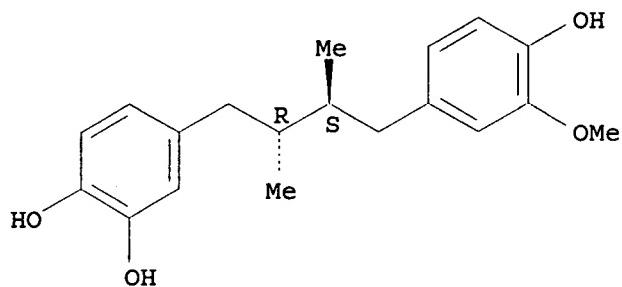
CMF C19 H24 O4

CDES 2:R*,S*

Relative stereochemistry.

Searcher : Shears 308-4994

08/882499



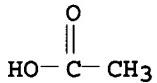
CM 2

CRN 67-56-1
CMF C H4 O

H₃C—OH

CM 3

CRN 64-19-7
CMF C2 H4 O2



RN 171439-77-3 CAPLUS

CN Phenol, 4(or 5)-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, 1-acetate, (R*,S*)- (9CI) (CA INDEX NAME)

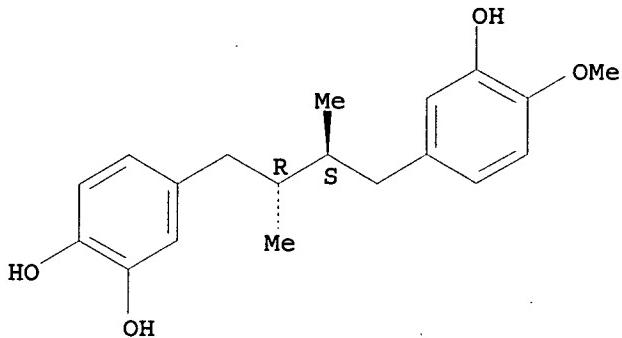
CM 1

CRN 171439-76-2
CMF C19 H24 O4
CDES 2:R*,S*

Relative stereochemistry.

Searcher : Shears 308-4994

08/882499



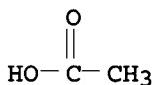
CM 2

CRN 67-56-1
CMF C H4 O

H₃C—OH

CM 3

CRN 64-19-7
CMF C2 H4 O2



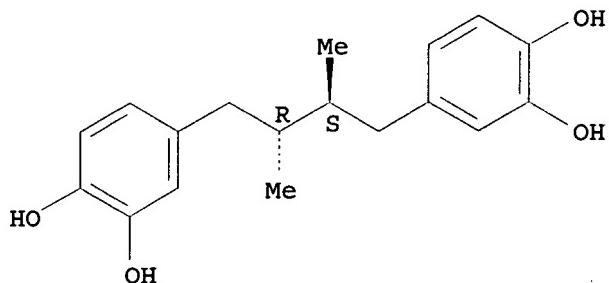
RN 171439-78-4 CAPLUS
CN 1,2-Benzenediol, 4-[4-[3(or 4)-(acetyloxy)-4(or 3)-methoxyphenyl]-2,3-dimethylbutyl]-, (R*,S*)- (9CI) (CA INDEX NAME)

CM 1

CRN 27686-84-6
CMF C18 H22 O4
CDES 2:R*,S*

Relative stereochemistry.

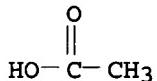
Searcher : Shears 308-4994



CM 2

CRN 67-56-1
CMF C H4 OH₃C—OH

CM 3

CRN 64-19-7
CMF C2 H4 O2

L12 ANSWER 20 OF 29 CAPLUS COPYRIGHT 1999 ACS
 ACCESSION NUMBER: 1995:464028 CAPLUS
 DOCUMENT NUMBER: 122:211984
 TITLE: Cell-to-cell contact not soluble factors mediate suppression of lymphocyte proliferation by bovine parainfluenza virus type 3
 AUTHOR(S): Basaraba, Randall J.; Laegreid, William W.; Brown, Peter R.; Silflow, Ron M.; Brown, Ruth A.; Leid, R. Wes
 CORPORATE SOURCE: College of Veterinary Medicine, Kansas State University, Manhattan, KS, 66506-5660, USA
 SOURCE: Viral Immunol. (1994), 7(3), 121-32
 CODEN: VIIMET; ISSN: 0882-8245
 DOCUMENT TYPE: Journal
 Searcher : Shears 308-4994

LANGUAGE: English

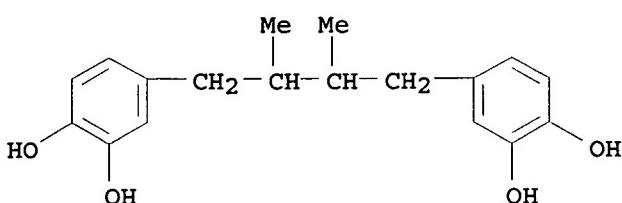
AB We have previously characterized the ability of parainfluenza virus type 3-infected (PIV-3) and noninfected bovine alveolar macrophages (BAM) to support lymphocyte proliferation. While uninfected macrophages support proliferation of lymphocytes stimulated with Con A (Con A), ovalbumin, and interleukin 2 (IL-2), lymphocyte [³H]thymidine incorporation was suppressed in the presence of PIV-3-infected BAM. Since viral infection of macrophages has been shown to alter arachidonic acid metab. and cytokine secretion, we have detd. if arachidonate metab. or the lack of IL-1 and IL-2 mediated the suppression of lymphocyte proliferation by PIV-3. Inhibition of arachidonic acid metab. failed to reverse the suppressive effect of viral infection as did supplementation of cultures with bovine recombinant IL-1 β , IL-2, or lymphocyte-conditioned medium. Further, lymphocytes proliferated normally when phys. sep'd. from virus infected BAM by a semipermeable membrane. Stimulation of lymphocytes in contact with infected BAM resulted in marked suppression of lymphocyte [³H]thymidine incorporation. Interactions between stimulated lymphocytes and PIV-3-infected BAM resulted in PIV-3 infection of lymphocytes. Virus infection of lymphocytes was confirmed ultrastructurally by the presence of characteristic parainfluenza virus inclusions and virus budding from lymphocyte plasma membranes. It was concluded that suppression of lymphocyte proliferation by PIV-3 is mediated in part by infection of stimulated lymphocytes during cell-to-cell contact with BAM.

IT 500-38-9, Nordihydroguaiaretic acid

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cell-to-cell contact not arachidonic acid metab. inhibitors or cytokines mediate suppression of lymphocyte proliferation by bovine parainfluenza virus type 3)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 21 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1995:403097 CAPLUS

DOCUMENT NUMBER: 122:177849

Searcher : Shears 308-4994

TITLE: E1A-3Y1 cell-specific toxicity of tea polyphenols and their killing mechanism

AUTHOR(S): Mitsui, Takeshi; Yamada, Koji; Yamashita, Kouhei; Matsuo, Noritaka; Okuda, Atsuyuki; Kimura, Genki; Sugano, Michihiro

CORPORATE SOURCE: Faculty Agriculture, Kyushu University, Higashi, 812, Japan

SOURCE: Int. J. Oncol. (1995), 6(2), 377-83

CODEN: IJONES; ISSN: 1019-6439

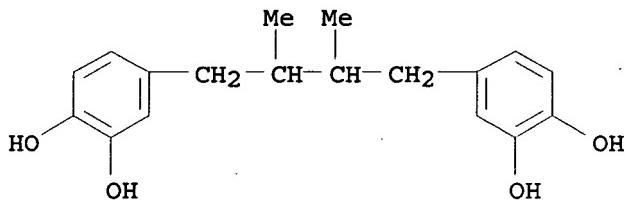
DOCUMENT TYPE: Journal

LANGUAGE: English

AB To screen carcinostatic components in foodstuffs, the toxicity of tea polyphenols was compared between rat 3Y1 diploid fibroblasts and a variety of their virally transformed cells. Among tea polyphenols tested, epigallocatechin gallate killed 3Y1 cells transformed by E1A gene of human adenovirus type 12 (E1A-3Y1 cells) at a 100 times lower concn. than the parental 3Y1 cells. Epigallocatechin gallate also exerted a strong E1A-3Y1 cell-specific toxicity, while epicatechin and epicatechin gallate did not. When the activity of three antioxidant enzymes was compared between 3Y1 and its transformants, catalase activity was markedly low in the latter, esp. in E1A-3Y1 cells, and the substrate of the enzyme, hydrogen peroxide, exerted a toxicity specific to this cell line. Then the inhibitory activities of various chems. on E1A-3Y1 cell-specific toxicity of phospholipids or catechol were examd. Among lipoxygenase inhibitors, all of the polyphenolic compds. inhibited the toxicity of phospholipids, but not a nonpolyphenolic inhibitor (clofibrate). Two phospholipase A2 inhibitors (dexamethasone and quinacrine) did not inhibit the toxicity. These results indicate that the triphenol structure of the B ring is essential for the E1A-3Y1 cell-specific toxicity of tea polyphenols, and that the decrease in catalase activity is partially responsible for the higher sensitivity of E1A-3Y1 cells against the polyphenols. The inhibitory effect of polyphenolic lipoxygenase inhibitors is ascribed at least in part to their antioxidant activities.

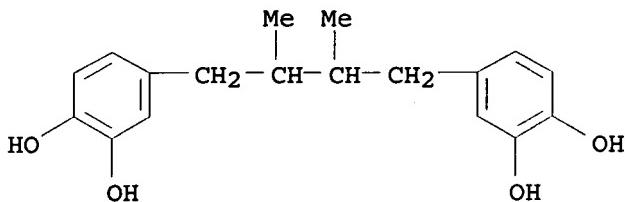
IT 500-38-9, NDGA
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (effect of lipoxygenase inhibitors and other chems. on cytotoxicity of phosphatidylcholine and catechol)

RN 500-38-9 CAPLUS
 CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 22 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1995:383556 CAPLUS
 DOCUMENT NUMBER: 122:150947
 TITLE: The non-steroidal anti-inflammatory drug,
 indomethacin, as an inhibitor of HIV replication
 AUTHOR(S): Bourinbaiar, Aldar S.; Lee-Huang, Sylvia
 CORPORATE SOURCE: Department of Biochemistry, New York University
 Medical Center, 550 First Avenue, New York, NY,
 10016, USA
 SOURCE: FEBS Lett. (1995), 360(1), 85-8
 CODEN: FEBLAL; ISSN: 0014-5793
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Indomethacin, a common non-steroidal anti-inflammatory drug (NSAID),
 has been used to treat rheumatoid arthritis. Although indomethacin
 has also been used as an immunopotentiator and symptomatic NSAID in
 AIDS, its effect on HIV replication is unknown. MT-4 lymphocytes
 were inoculated with HIV in the presence of indomethacin and tested
 for p24 expression by ELISA. The 50% inhibition (IC50) was 10
 mu.M, corresponding to plasma levels after administration of 50 mg
 oral indomethacin. The antiviral effect appears to be
 specific since no toxicity has been obsd. at the IC50 dose, and
 unrelated NSAIDs have not shown the activity at clin. doses.
 Indomethacin may, thus, represent a new class of anti-HIV drug.
 IT 500-38-9, NDGA
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effect of NSAIDs on HIV infection)
 RN 500-38-9 CAPLUS
 CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
 INDEX NAME)



L12 ANSWER 23 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1994:473911 CAPLUS

DOCUMENT NUMBER: 121:73911

TITLE: Inhibitors of arachidonic acid metabolites for preventing neurological damage, and screening method for neuroprotectants

INVENTOR(S): Bernton, Edward W.; Jett, Marti; Gendelman, Howard

PATENT ASSIGNEE(S): United States Department of the Army, USA

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9412667	A1	19940609	WO 93-US11542	19931129
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			US 92-982656	19921127
			US 93-61970	19930902

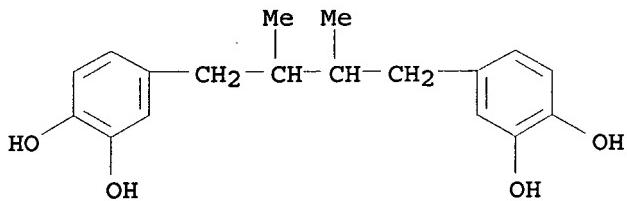
AB A method is provided for treating encephalitis or encephalopathy secondary to CNS infection by administration of therapeutically effective amts. of compns. which inhibit the release of platelet activation factor and/or arachidonate metabolites. Compns. are disclosed contg. e.g. 11-nor-.DELTA.8-tetrahydrocannabinol-9-carboxylic acid or nordihydroguaiaretic acid. Also provided are methods for screening for compds. that have neuroprotective activity; the methods comprise infecting monocytes or lymphocytes with an infectious organism known to cause neural damage, adding the resulting infected culture to a culture of astrocyte cells, adding a test compd., allowing sufficient time to pass for the prodn. of TNF-alpha, withdrawing aliquots from the supernatant of the culture, adding the aliquots to cultures of neural cells and identifying which supernatants impart a neuroprotective effect.

IT 500-38-9, Nordihydroguaiaretic acid

Searcher : Shears 308-4994

08/882499

RL: BIOL (Biological study)
(neuroprotectant compn. contg.)
RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
INDEX NAME)



L12 ANSWER 24 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1994:450038 CAPLUS
DOCUMENT NUMBER: 121:50038
TITLE: Antioxidants inhibit stimulation of HIV transcription
AUTHOR(S): Staal, Frank J. T.; Roederer, Mario; Raju, Paul A.; Anderson, Michael T.; Ela, Stephen W.; Herzenberg, Leonard A.; Herzenberg, Leonore A.
CORPORATE SOURCE: Dep. Genet., Stanford Univ. Sch. Med., Stanford, CA, 94305, USA
SOURCE: AIDS Res. Hum. Retroviruses (1993), 9(4), 299-306
CODEN: ARHRE7; ISSN: 0889-2229
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In studies presented here, the authors demonstrate that antioxidants regulate NF- κ B activation and signal transduction pathways leading to HIV expression. The authors show (1) that N-acetyl-L-cysteine (NAC), an antioxidant and an efficient glutathione (GSH) precursor, inhibits NF- κ B activation and HIV expression under conditions in which GSH is depleted and NAC cannot be converted to GSH, (2) that the D-stereoisomer of NAC and a wide variety of chem. unrelated antioxidants also inhibit NF- κ B activation and/or transcription directed by the HIV LTR, and (3) that depletion of GSH, the principal intracellular antioxidant, augments HIV prodn. in an acute infection model. Taken together, these findings suggest direct antioxidant action as the mechanism for inhibition of HIV transcription by NAC. They also confirm that GSH, acting in its capacity as an antioxidant, regulates HIV expression and that exogenous antioxidants can potentiate this regulation.

IT 500-38-9, Nordihydroguaiaretic acid
Searcher : Shears 308-4994

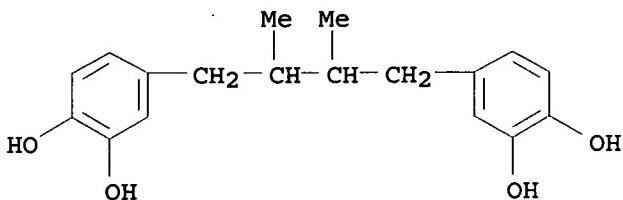
08/882499

RL: BIOL (Biological study)

(HIV transcription and replication inhibition by, as antioxidant)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
INDEX NAME)



L12 ANSWER 25 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1991:115083 CAPLUS

DOCUMENT NUMBER: 114:115083

TITLE: Use of fatty acids or other compounds for the treatment of diseases associated with cytokines, such as alleviation of symptoms of influenza or the common cold

INVENTOR(S): Tan, Yin Hwee; Lim, Louis

PATENT ASSIGNEE(S): National University of Singapore, Singapore

SOURCE: Eur. Pat. Appl., 17 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 396251	A2	19901107	EP 90-303361	19900329
EP 396251	A3	19920708		
R: CH, DE, FR, GB, LI, NL				
JP 03083933	A2	19910409	JP 89-220144	19890825
PRIORITY APPLN. INFO.:			GB 89-7308	19890331
			JP 89-220144	19890825

AB Arachidonic acid (I), an arachidonic acid analog, nordihydroguaiaretic acid (II), ketoconazole (III), or quercetin or used in the prepn. of a medicament for use in the treatment of a disease state assocd. with the endogenous presence and/or prodn. of a cytokine. The compds. of the invention can be used to alleviate the symptoms of the common cold or influenza. Thus, 50 .mu.M I, 50 .mu.M II, and 100 .mu.M III inhibited the antiviral state induced by .alpha.- or .beta.-interferon by >90%; 50 .mu.M I also inhibited the antiviral state induced by

Searcher : Shears 308-4994

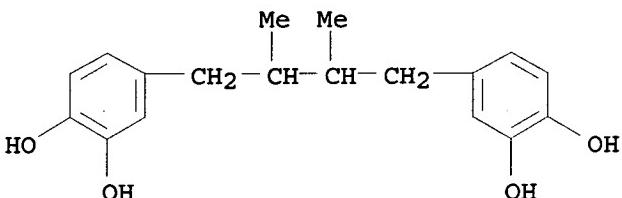
.gamma.-interferon by .gtoreq.80%. Data are presented that suggest that I and other compds. of the invention can diminish the binding of ligands (interferon) to their receptors.

IT 500-38-9, Nordihydroguaiaretic acid

RL: BIOL (Biological study)
(for cytokine-assocd. disease treatment)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 26 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1991:58721 CAPLUS

DOCUMENT NUMBER: 114:58721

TITLE: Inhibitors of the lipoxygenase pathway
specifically block orthopoxvirus replication

AUTHOR(S): Palumbo, G. J.; Buller, R. M. L.

CORPORATE SOURCE: Lab. Viral. Dis., Natl. Inst. Allergy and
Infect. Dis., Bethesda, MD, 20892, USA

SOURCE: Virology (1991), 180(1), 457-63

CODEN: VIRLAX; ISSN: 0042-6822

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhibitors of arachidonic acid metab., 5,8,11,14-eicosatetraynoic acid (ETYA), BW755c, and nordihydroguaiaretic acid, were found to specifically interfere with the replication of cowpox virus (an orthopoxvirus) both in vivo and in vitro. Further studies in vitro showed that the drugs ETYA and BW755c were effective in inhibiting the replication of two addnl. orthopoxviruses, ectromelia and vaccinia viruses, but not human parainfluenza virus-3. In ETYA-treated and cowpox virus-infected cells, early and late gene expression were near normal levels, whereas the assembly of virus-specific membranes was severely reduced. These results are compatible with a model of orthopoxvirus replication that has an obligate requirement for arachidonic acid or one of its metabolic forms, possibly in the assembly of virus-specific membranes.

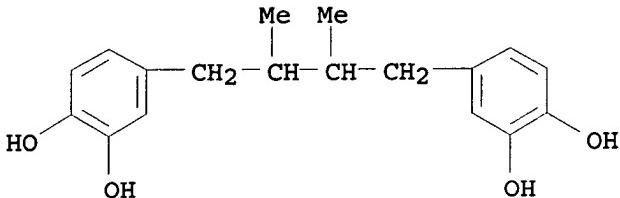
IT 500-38-9, Nordihydroguaiaretic acid

RL: BIOL (Biological study)
(replication of orthopoxvirus inhibition by)

Searcher : Shears 308-4994

08/882499

RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
INDEX NAME)



L12 ANSWER 27 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1987:451447 CAPLUS
DOCUMENT NUMBER: 107:51447
TITLE: The effect of modulating the synthesis of arachidonic acid cascade products on HSV lesion recurrence
AUTHOR(S): Yates, F.; Centifanto, Y. M.; Caldwell, D. R.
CORPORATE SOURCE: Sch. Med., Tulane Univ., New Orleans, LA, 70112, USA
SOURCE: Curr. Eye Res. (1987), 6(1), 99-104
CODEN: CEYRDM; ISSN: 0271-3683

DOCUMENT TYPE: Journal

LANGUAGE: English

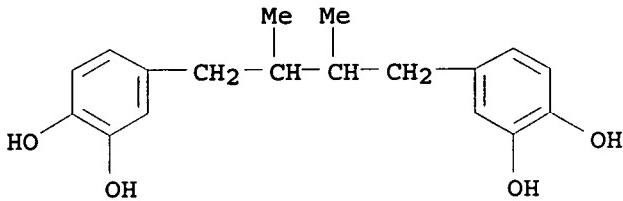
AB Meclofenamate, nordihydroguaiaretic acid (NDGA), and chlorpromazine, which inhibit various products of the arachidonic acid cascade, were compared with saline and corticosteroids in mouse ear models of herpes simplex virus (HSV) recurrence.

The relative efficacy in lesion redn. between groups by day 5 post recurrence induction (PRI) is: meclofenamate>steroid = chlorpromazine>NDGA>saline. Meclofenamate, steroid, and chlorpromazine significantly reduced lesions when compared with the saline-treated control mice. NDGA did not significantly reduce lesions by day 5 PRI. Mechanisms of drug action are considered.

IT 500-38-9, Nordihydroguaiaretic acid

RL: BIOL (Biological study)
(herpes simples virus lesion recurrence
response to, arachidonic metabolite modulation in relation to)

RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
INDEX NAME)



L12 ANSWER 28 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1986:604506 CAPLUS

DOCUMENT NUMBER: 105:204506

TITLE: Inhibition of 12-O-tetradecanoylphorbol-13 acetate-induced induction of Epstein-Barr virus early antigen in Raji cells by some inhibitors of tumor promotion

AUTHOR(S): Saito, Yutaka; Okamoto, Hitoshi; Mizusaki, Shigenobu; Yoshida, Daisuke

CORPORATE SOURCE: Cent. Res. Inst., Japan Tob. Inc., Yokohama, 227, Japan

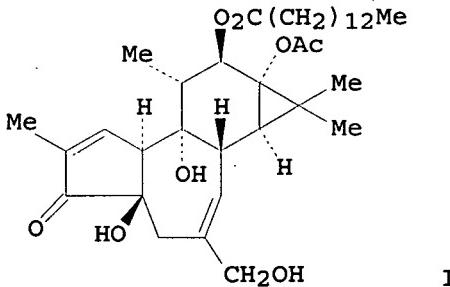
SOURCE: Cancer Lett. (Shannon, Ireln.) (1986), 32(2), 137-44

CODEN: CALEDQ; ISSN: 0304-3835

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The effects of some compds., which have been reported to inhibit tumor promotion in vivo, on the induction of the early antigen (EA) of Epstein-Barr virus (EBV) by TPA (I) [16561-29-8] in Raji cells were examd. The inhibitors of the cascade process involving arachidonic acid [506-32-1], indomethacin [53-86-1], nordihydroguaiaretic acid [500-38-9], phenidone [92-43-3] and p-bromophenacyl bromide [99-73-0], effectively inhibited EBV-EA induction by TPA. Two flavonoids, morin

Searcher : Shears 308-4994

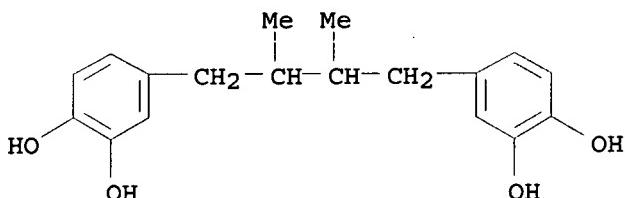
[480-16-0] and kaempferol [520-18-3] also inhibited EA induction. Among antioxidants, butylated hydroxytoluene [128-37-0] effectively inhibited EA induction, though .alpha.-tocopherol [59-02-9] did not show any inhibition of EA induction at concns. of up to 150 .mu.g/mL. N-(6-Aminohexyl)-5-chloro-1-naphthalenesulfonamide [65595-90-6], a calmodulin antagonist, and esculentin [305-01-1] showed inhibitory effects on EA induction, though slight cytotoxicity was obsd. L-1-p-Tosylamino-2-phenylethyl chloromethyl ketone [402-71-1], a protease inhibitor, showed cytotoxicity and no specific inhibition of EA induction. Five kinds of steroids, cortisone [53-06-5], hydrocortisone [50-23-7], prednisolone [50-24-8], dexamethasone [50-02-2] and fluocinolone acetonide [67-73-2] showed no inhibitory effect on EA induction at concns. <100 .mu.g/mL. In addn., the relationship between the inhibition of EBV-EA induction and that of tumor promotion is discussed.

IT 500-38-9

RL: BIOL (Biological study)
 (TPA-induced Epstein-Barr virus early antigen in Raji
 cells response to)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
 INDEX NAME)



L12 ANSWER 29 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1986:61594 CAPLUS

DOCUMENT NUMBER: 104:61594

TITLE: Reversal of feline retroviral suppression by
 indomethacinAUTHOR(S): Lewis, Mark G.; Fertel, Richard H.; Olsen,
 Richard G.CORPORATE SOURCE: Dep. Vet. Pathobiol., Ohio State Univ.,
 Columbus, OH, 43210, USASOURCE: Leuk. Res. (1985), 9(12), 1451-6
 CODEN: LEREDD; ISSN: 0145-2126

DOCUMENT TYPE: Journal

LANGUAGE: English

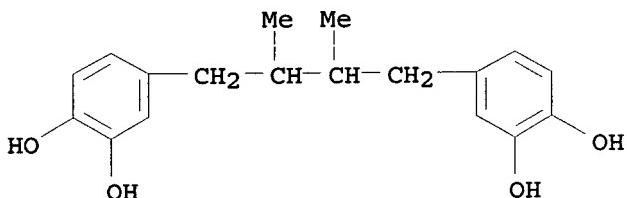
AB The immunosuppressive effect of feline leukemia virus (FeLV) and its 15,000-dalton envelope protein (p15E) was studied to
 Searcher : Shears 308-4994

det. if the mechanism of action was due to an increase in prostaglandin prodn. Exogenous PGE1 [745-65-3] and PGE2 [363-24-6] inhibited the normal Con A response of feline peripheral blood lymphocytes (PBL). The addn. of the cyclooxygenase [39391-18-9] inhibitor indomethacin [53-86-1] to cells incubated with FeLV or FeLV p15E and Con A completely abrogated the viral suppressive effects. This reversal was titratable and time-dependent. Other nonsteroidal anti-inflammatory inhibitors (NSAI) had similar actions. Indomethacin was also able to increase the suppressed Con A response of PBL from FeLV-infected cats. Upon measurement of PGE2 levels from PBL cultured with FeLV, there was a decrease in PGE2 accumulation assocd. with FeLV presence during the 1st 24 h of culture. These findings indicate that FeLV does not cause its immunosuppressive effects by increasing PG prodn. and suggest that indomethacin and the other tested NSAI do not produce their effect by PG inhibition.

IT 500-38-9

RL: BIOL (Biological study)
 (feline leukemia virus-induced immunosuppression
 inhibition by)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA
 INDEX NAME)

FILE 'REGISTRY' ENTERED AT 16:52:28 ON 03 JUN 1999
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 1999 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 28 MAY 99 HIGHEST RN 223764-44-1
 DICTIONARY FILE UPDATES: 03 JUN 99 HIGHEST RN 223764-44-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

Please note that search-term pricing does apply when
 conducting SmartSELECT searches.

=> d que

L13 37 SEA FILE=REGISTRY ABB=ON PLU=ON (500-38-9/BI OR
 Searcher : Shears 308-4994

08/882499

171204-38-9/BI OR 171204-39-0/BI OR 171204-41-4/BI OR
171204-43-6/BI OR 178557-46-5/BI OR 24150-24-1/BI OR
27686-84-6/BI OR 54473-24-4/BI OR 66322-34-7/BI OR
119584-39-3/BI OR 171204-42-5/BI OR 171439-75-1/BI OR
171439-76-2/BI OR 171439-77-3/BI OR 171439-78-4/BI OR
174155-42-1/BI OR 174155-43-2/BI OR 174155-45-4/BI OR
174291-51-1/BI OR 174291-52-2/BI OR 174291-53-3/BI OR
174291-54-4/BI OR 174291-55-5/BI OR 174291-56-6/BI OR
178557-47-6/BI OR 178557-48-7/BI OR 178557-49-8/BI OR
178557-50-1/BI OR 178557-51-2/BI OR 178557-52-3/BI OR
178557-53-4/BI OR 205758-62-9/BI OR 212325-18-3/BI OR
212325-19-4/BI OR 71113-15-0/BI OR 72730-20-2/BI)

=> fil caold; s 113

FILE 'CAOLD' ENTERED AT 16:53:11 ON 03 JUN 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 1999 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, and patent assignees are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L14 20 L13

=> d 1-20; fil uspat; s 113

L14 ANSWER 1 OF 20 COPYRIGHT 1999 ACS
AN CA65:12772e CAOLD
TI preservation of olive husks with antioxidants and fungistats
AU Savastano, Giulio; Castorina, S.
IT 121-79-9 500-38-9

L14 ANSWER 2 OF 20 COPYRIGHT 1999 ACS
AN CA65:9611e CAOLD
TI anal. detn. of 90Sr in foods
AU Davis, Sidney
IT 121-79-9 500-38-9

Searcher : Shears 308-4994

- L14 ANSWER 3 OF 20 COPYRIGHT 1999 ACS
AN CA65:7893c CAOLD
TI sepn. and detection of antioxidants in vitamin A oil and vegetable oil by thinlayer chromatography
AU Ishikawa, Seiji; Katsui, G.
IT 500-38-9 2486-02-4
- L14 ANSWER 4 OF 20 COPYRIGHT 1999 ACS
AN CA65:6196c CAOLD
TI changes of lard resulting from the addn. of antioxidants during heating
AU Sedlacek, Bohuslav A. J.
IT 121-79-9 500-38-9 1166-52-5
- L14 ANSWER 5 OF 20 COPYRIGHT 1999 ACS
AN CA65:4531e CAOLD
TI kinetic method for the detn. of the activity of antioxidants for confectionery production
AU Dremina, N. V.; Li, L.; Gurova-Kuperman, L. A.
IT 500-38-9 1166-52-5
- L14 ANSWER 6 OF 20 COPYRIGHT 1999 ACS
AN CA65:2527h CAOLD
TI complexity of .alpha.-crystallin
AU Bon, Willem F.; Ruttenberg, G. J. C. M.
IT 59-02-9 74-31-7 90-34-6 91-53-2 123-28-4
225-51-4 500-38-9 2498-75-1 2896-55-1 4345-03-3
7724-47-2
- L14 ANSWER 7 OF 20 COPYRIGHT 1999 ACS
AN CA64:17375g CAOLD
TI oxidn. of phenols - (III) stoichiometries for the oxidn. of some substituted phenols with peroxy radicals
AU Horswill, E. C.; Howard, J. A.; Ingold, K. U.
IT 91-10-1 93-51-6 96-76-4 98-29-3 128-39-2
500-38-9 527-60-6 616-55-7 2219-82-1 2409-55-4
- L14 ANSWER 8 OF 20 COPYRIGHT 1999 ACS
AN CA64:17361g CAOLD
TI stability of fat bases applied in galenic preps. - (III)
antioxidants most frequently used in practice and their chem. properties
AU Wisniewski, Wladyslaw; Golucki, Z.
IT 121-79-9 500-38-9 1034-01-1 1166-52-5 25013-16-5
- L14 ANSWER 9 OF 20 COPYRIGHT 1999 ACS
AN CA64:9890b CAOLD
TI antioxidants for high polymers - (I) inhibiting effects of
Searcher : Shears 308-4994

08/882499

antioxidants on autoxidn. of polyethylene, (II) inhibiting effects
of antioxidants on autoxidn. of polypropylene

AU Yoshida, Zenichi; Miyoshi

IT 74-31-7 80-05-7 88-58-4 90-66-4 93-46-9
101-87-1 119-47-1 147-47-7 500-38-9 2781-09-1
3568-26-1 7005-40-5 7005-43-8 7005-44-9 7005-45-0
7580-46-3

L14 ANSWER 10 OF 20 COPYRIGHT 1999 ACS

AN CA64:5373b CAOLD

TI characteristics of eggplant and avocado polyphenolases

AU Knapp, Frederick W.

IT 103-85-5 148-18-5 331-39-5 500-38-9

L14 ANSWER 11 OF 20 COPYRIGHT 1999 ACS

AN CA64:3951a CAOLD

TI bioassay for antioxidants based on protection of Tetrahymena
pyriformis from the photodynamic toxicity of benzo(.alpha.)pyrene

AU Epstein, Samuel S.; Saporoschetz, I. B.; Small, M.; Park, W.;
Mantel, N.

IT 50-63-5 50-81-7 51-85-4 52-89-1 54-85-3
54-88-6 55-80-1 56-10-0 59-02-9 59-52-9 61-73-4
61-82-5 65-49-6 68-26-8 74-31-7 79-74-3 88-26-6
88-32-4 90-34-6 91-53-2 94-13-3 97-56-3 99-76-3
101-70-2 102-71-6 110-44-1 111-17-1 118-42-3 119-11-9
119-13-1 120-47-8 121-00-6 122-39-4 123-28-4 123-31-9
127-40-2 131-56-6 136-36-7 148-03-8 490-79-9
500-38-9 526-83-0 582-08-1 621-90-9 680-31-9
991-84-4 991-85-5 992-47-2 992-48-3 1421-63-2 1709-70-2
1948-33-0 2058-66-4 2058-67-5 2481-94-9 2512-56-3
2896-55-1 2929-94-4 2985-59-3 3010-57-9 3135-18-0
3147-76-0 3312-50-3 3731-39-3 3732-90-9 4345-03-3
5014-86-8 5302-41-0 5891-06-5 6010-34-0 6029-97-6
6030-03-1 6922-60-7 7050-06-8 16971-82-7 68108-20-3
106979-54-8

L14 ANSWER 12 OF 20 COPYRIGHT 1999 ACS

AN CA64:3282d CAOLD

TI use of polyacrylamide for the purification of diffusion juices of
caffeine

AU Filippos'yants, T. T.; Sandomirskaya, G. A.; Pozdnyakova, Z. E.

IT 51-40-1 59-30-3 62-54-4 68-89-3 71-27-2
127-65-1 130-37-0 133-15-3 300-08-3 314-19-2
500-38-9 591-64-0 814-80-2 2944-65-2

L14 ANSWER 13 OF 20 COPYRIGHT 1999 ACS

AN CA63:15050b CAOLD

TI identification of antioxidants in plastics

AU Heide, Ruurd F. van der; Maagdenburg, A. C.; Neut, J. H. van der
Searcher : Shears 308-4994

08/882499

IT 96-69-5 111-17-1 121-79-9 123-28-4 500-38-9
693-36-7 1034-01-1 1166-52-5 1335-16-6 1421-63-2 1709-70-2
4066-02-8 28852-17-7

L14 ANSWER 14 OF 20 COPYRIGHT 1999 ACS
AN CA63:13631g CAOLD
TI southern pea lipoxidase
AU Knapp, Frederick W.
IT 500-38-9

L14 ANSWER 15 OF 20 COPYRIGHT 1999 ACS
AN CA63:10256b CAOLD
TI inhibition of soybean lipoxidase
AU Blain, John A.; Shearer, G.
IT 500-38-9 1191-85-1 2012-14-8 4102-60-7 4102-62-9
4184-92-3 4184-93-4 4184-96-7

L14 ANSWER 16 OF 20 COPYRIGHT 1999 ACS
AN CA62:16804a CAOLD
TI effect of antioxidants on the liberation of fatty acids from adipose tissues
AU Placer, Zdenek; Petrasek, R.; Veselkova, A.; Rath, R.
IT 99-24-1 144-12-7 500-38-9 1034-01-1

L14 ANSWER 17 OF 20 COPYRIGHT 1999 ACS
AN CA55:14753b CAOLD
TI feed supplement for hens
AU Koffler, Maximilian
DT Patent
IT 66322-34-7 112867-79-5

L14 ANSWER 18 OF 20 COPYRIGHT 1999 ACS
AN CA55:4468e CAOLD
TI intermediates necessary in the synthesis of resinols and derivs. -
(V), (VI)
AU Traverso, Giorgio
IT 721-42-6 833-67-0 1835-02-5 4650-69-5 4650-71-9
4687-37-0 5701-82-6 51487-58-2 53293-07-5 66322-34-7
101499-83-6 102454-96-6 102655-73-2 102761-86-4 102890-88-0
103042-42-8 103239-13-0 111612-07-8 112867-79-5
115322-45-7 115386-03-3 124117-73-3

L14 ANSWER 19 OF 20 COPYRIGHT 1999 ACS
AN CA51:17851i CAOLD
TI meso-dihydroguaiaretic acid and its derivs.
AU Schrecker, Anthony W.
IT 500-40-3 5507-27-7 5701-82-6 7461-04-3 24289-99-4
42923-56-8 63339-53-7 66322-34-7 93578-43-9 93578-48-4
93609-04-2 95810-13-2 102757-68-6 102758-58-7 103402-11-5
Searcher : Shears 308-4994

08/882499

112867-79-5 121271-89-4 124117-73-3

L14 ANSWER 20 OF 20 COPYRIGHT 1999 ACS
AN CA51:4330f CAOLD
TI abs. configuration of dihydroguaiaretic acid
AU Carnmalm, Bernt
IT 5701-82-6 7475-92-5 13545-04-5 26979-55-5 58372-16-0
66322-34-7 92203-55-9 100523-76-0 101257-25-4 102471-96-5
112867-79-5

=> d his 115- ful; d 1-13 ibib abs

(FILE 'USPATFULL' ENTERED AT 16:53:20 ON 03 JUN 1999)

L15 43 SEA ABB=ON PLU=ON L13
L16 13 SEA ABB=ON PLU=ON L15 AND (ANTIVIR? OR VIRUS? OR
VIRAL? OR (HSV OR HV) (S)HERPES? OR HERPES?)

L16 ANSWER 1 OF 13 USPATFULL
ACCESSION NUMBER: 1998:143662 USPATFULL
TITLE: Nontoxic extract of Larrea tridentata and method
of making same
INVENTOR(S): Sinnott, Robert A., Chandler, AZ, United States
Clark, W. Dennis, Phoenix, AZ, United States
DeBoer, Kenneth Frank, Belgrade, MT, United
States
PATENT ASSIGNEE(S): Larreacorp, Ltd., Chandler, AZ, United States
(U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5837252	19981117
APPLICATION INFO.:	US 96-726686	19961007 (8)
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Witz, Jean C.	
ASSISTANT EXAMINER:	Hanley, Susan	
LEGAL REPRESENTATIVE:	Benson, David K.; Nichols, Steven L.	
NUMBER OF CLAIMS:	8	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)	
LINE COUNT:	692	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A nontoxic, therapeutic agent having pharmacological activity comprising concentrated extract of Larrea tridentata plant material and ascorbic acid, an ascorbic acid ester, an ascorbic acid salt, butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulfide, hypophosphorous acid, monothioglycerol, potassium bisulfite, propyl gallate, sodium bisulfite, sodium hydrosulfite, sodium thiosulfate, sulfur dioxide, sulfurous acid, a tocopherol, or vitamin E is made by a process in which the plant

Searcher : Shears 308-4994

material is extracted using an organic solvent, preferably acetone, and is then saturated with one of the listed reducing agents acid to reduce the toxic NDGA quinone, which naturally occurs in the plant material, to NDGA itself. Additional amounts of ascorbic acid, an ascorbic acid ester, an ascorbic acid salt, butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulfide, hypophosphorous acid, monothioglycerol, potassium bisulfite, propyl gallate, sodium bisulfite, sodium hydrosulfite, sodium thiosulfate, sulfur dioxide, sulfurous acid, a tocopherol, or vitamin E may be added to the extract to inhibit the natural oxidation of the NDGA into the toxic NDGA quinone in vivo, or during processing or storage. The resulting extract is useful in the treatment of viral diseases caused by viruses from the Herpesviridae family or viruses which require the Sp1 class of proteins to initiate viral replications. The resulting compound can also be used as an anti-inflammatory when the inflammatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize NDGA as a therapeutic agent or a food additive.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 2 OF 13 USPATFULL

ACCESSION NUMBER: 97:122847 USPATFULL
 TITLE: Treatment for biological damage using a colony stimulating factor and a biological modifier
 INVENTOR(S): Zimmerman, Robert, Lafayette, CA, United States
 Marafino, Jr., Benedict J., San Francisco, CA,
 United States
 PATENT ASSIGNEE(S): Chiron Corporation, Emeryville, CA, United States
 (U.S. corporation)

PATENT INFORMATION:	NUMBER	DATE
	-----	-----
APPLICATION INFO.:	US 5702697	19971230
RELATED APPLN. INFO.:	US 95-457629	19950601 (8)
	Continuation of Ser. No. US 94-289844, filed on 12 Aug 1994, now patented, Pat. No. US 5508031 which is a continuation of Ser. No. US 93-49070, filed on 16 Apr 1993, now abandoned which is a continuation of Ser. No. US 90-626975, filed on 12 Dec 1990, now abandoned which is a division of Ser. No. US 89-399386, filed on 25 Aug 1989, now patented, Pat. No. US 4985241 which is a continuation of Ser. No. US 87-113643, filed on 26 Oct 1987, now abandoned which is a continuation-in-part of Ser. No. US 86-933475, filed on 21 Nov 1986, now abandoned	
	Searcher : Shears 308-4994	

DOCUMENT TYPE: Utility
 PRIMARY EXAMINER: Ulm, John
 ASSISTANT EXAMINER: Mertz, Prema
 LEGAL REPRESENTATIVE: Gass, David A.; Savereide, Paul B.; Blackburn, Robert P.
 NUMBER OF CLAIMS: 32
 EXEMPLARY CLAIM: 1
 LINE COUNT: 1705

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Damage to cells, tissue and other body parts in a mammalian host may be treated by using a colony stimulating factor in conjunction with at least one biological modifier, which may be a free radical scavenger or a metabolic inhibitor. The biological modifier is preferably uric acid, buthionine sulphoximine, vitamin C, aspirin, or nordihydroguaiaretic acid. Such a combination may be used to treat, for example, cancer, infectious diseases, and damage caused by radiation therapy, high oxygen tension, and chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 3 OF 13 USPATFULL
 ACCESSION NUMBER: 97:122844 USPATFULL
 TITLE: Compositions for treating corns, calluses and warts
 INVENTOR(S): Chamness, Thomas W., Memphis, TN, United States
 PATENT ASSIGNEE(S): Schering-Plough HealthCare Products, Inc., United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5702694	19971230
	WO 9505156	19950223
APPLICATION INFO.:	US 96-596219	19960212 (8)
	WO 94-US8315	19940811 19960212 PCT 371 date 19960212 PCT 102(e) date
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 93-107553, filed on 17 Aug 1993	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Page, Thurman K.	
ASSISTANT EXAMINER:	Shelborne, Kathryne E.	
LEGAL REPRESENTATIVE:	Boxer, Matthew; Maitner, John	
NUMBER OF CLAIMS:	12	
EXEMPLARY CLAIM:	1	
LINE COUNT:	934	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Topical compositions for the treatment of corns, calluses and warts comprising a benzenediol or a substituted 1,2-benzenediol and a pharmaceutically acceptable carrier, are described.

Searcher : Shears 308-4994

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 4 OF 13 USPATFULL

ACCESSION NUMBER: 97:83609 USPATFULL

TITLE: Treatment for biological damage using tumor necrosis factor and a free-radical scavenger

INVENTOR(S): Zimmerman, Robert, Lafayette, CA, United States
Marafino, Jr., Benedict J., San Francisco, CA,
United States

PATENT ASSIGNEE(S): Chiron Corporation, Emeryville, CA, United States
(U.S. corporation)

NUMBER	DATE
-----	-----

PATENT INFORMATION: US 5667776 19970916

APPLICATION INFO.: US 95-456947 19950601 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 94-289844, filed on 12 Aug 1994, now patented, Pat. No. US 5508031 which is a continuation of Ser. No. US 93-49070, filed on 16 Apr 1993, now abandoned which is a continuation of Ser. No. US 90-626975, filed on 12 Dec 1990, now abandoned which is a division of Ser. No. US 89-399386, filed on 25 Aug 1989, now patented, Pat. No. US 4985241 which is a continuation of Ser. No. US 87-113643, filed on 26 Oct 1987, now abandoned which is a continuation-in-part of Ser. No. US 86-933475, filed on 21 Nov 1986, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Ulm, John

ASSISTANT EXAMINER: Mertz, Prema

LEGAL REPRESENTATIVE: Gass, David A.; Savereide, Paul B.; Blackburn, Robert P.

NUMBER OF CLAIMS: 30

EXEMPLARY CLAIM: 1

LINE COUNT: 1648

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Damage to cells, tissue and other body parts in a mammalian host may be treated by using a tumor necrosis factor in conjunction with at least one biological modifier, which may be a free radical scavenger or a metabolic inhibitor. The biological modifier is preferably uric acid, buthionine sulphoximine, vitamin C, aspirin, or nordihydroguaiaretic acid. Such a combination may be used to treat, for example, cancer, infectious diseases, and damage caused by radiation therapy, high oxygen tension, and chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

08/882499

L16 ANSWER 5 OF 13 USPATFULL

ACCESSION NUMBER: 97:78478 USPATFULL
TITLE: Compounds for the suppression of HIV Tat transactivation
INVENTOR(S): Huang, Ru Chih C., Baltimore, MD, United States
Gnabre, John N., Baltimore, MD, United States
PATENT ASSIGNEE(S): The Johns Hopkins University, Baltimore, MD,
United States (U.S. corporation)

NUMBER DATE

PATENT INFORMATION: US 5663209 19970902
APPLICATION INFO.: US 96-627588 19960404 (8)
RELATED APPLN. INFO.: Division of Ser. No. US 94-316341, filed on 30
Sep 1994

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Rollins, John W.

LEGAL REPRESENTATIVE: Cushman Darby & Cushman IP Group Pillsbury
Madison & Sutro LLP

NUMBER OF CLAIMS: 11

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 765

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention reveals the isolation, purification and characterization from the creosote bush *Larrea tridentata* of compounds of the structural formula: ##STR1## where R.₁, R.₂, R.₃ and R.₄ are each selected from the group consisting of HO--, CH.₂.₃O-- and CH.₂.₃(C.dbd.O)O--, provided that R.₁, R.₂, R.₃ and R.₄ are not each HO-- simultaneously. Each compound is a derivative of 1,4-bis-(3,4-dihydroxyphenyl)-2,3-dimethylbutane (nordihydroquaiaretic acid, NDGA). In addition, NDGA and each derivative can be used in a method to suppress Tat transactivation of a lentivirus, including the HIV virus, in a cell by administering NDGA or a derivative of NDGA to the cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 6 OF 13 USPATFULL

ACCESSION NUMBER: 96:68050 USPATFULL
TITLE: Treatment of multidrug resistant diseases
INVENTOR(S): Howell, Stephen, Del Mar, CA, United States
Khandwala, Atul, Edgewater, NJ, United States
Sachdey, Om P., New City, NY, United States
Smith, Charles G., Rancho Santa Fe, CA, United States
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., Tarrytown, NY,
United States (U.S. corporation)
Searcher : Shears 308-4994

08/882499

	NUMBER	DATE
PATENT INFORMATION:	US 5541232	19960730
APPLICATION INFO.:	US 94-264740	19940623 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 93-81663, filed on 23 Jun 1993, now patented, Pat. No. US 5409690	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Criares, Theodore J.	
LEGAL REPRESENTATIVE:	Weiser & Associates	
NUMBER OF CLAIMS:	35	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 5 Drawing Page(s)	
LINE COUNT:	964	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and composition for treating multidrug resistance in a mammal, in which the composition includes NDGA or an analog of NDGA in accordance with the following formula: ##STR1## wherein R.sub.1 and R.sub.2 are independently H, lower alkyl or lower acyl;

R.sub.3, R.sub.4, R.sub.5, and R.sub.6 are independently H or lower alkyl;

R.sub.7, R.sub.8 and R.sub.9 are independently H, hydroxy, lower alkoxy or lower acyloxy; and

R.sub.10, R.sub.11, R.sub.12 and R.sub.13 are independently H or lower alkyl, in a pharmaceutically acceptable vehicle.

The method is particularly suitable for administering an antineoplastic agent, and the composition includes the combination of NDGA, or an analog with such an antineoplastic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 7 OF 13 USPATFULL
ACCESSION NUMBER: 96:31583 USPATFULL
TITLE: Method for treating biological damage using a free-radical scavenger and interleukin-2
INVENTOR(S): Zimmerman, Robert, Lafayette, CA, United States
Marafino, Jr., Benedict J., San Francisco, CA,
United States
PATENT ASSIGNEE(S): Cetus Oncology Corporation, Emeryville, CA,
United States (U.S. corporation)

NUMBER	DATE
Searcher : Shears	308-4994

08/882499

PATENT INFORMATION: US 5508031 19960416
APPLICATION INFO.: US 94-289844 19940812 (8)
RELATED APPLN. INFO.: Continuation of Ser. No. US 93-49070, filed on 16 Apr 1993, now abandoned which is a continuation of Ser. No. US 90-626975, filed on 12 Dec 1990, now abandoned which is a division of Ser. No. US 89-399386, filed on 25 Aug 1989, now patented, Pat. No. US 4985241 which is a continuation of Ser. No. US 87-113643, filed on 26 Oct 1987, now abandoned which is a continuation-in-part of Ser. No. US 86-933475, filed on 21 Nov 1986, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Walsh, Stephen G.

LEGAL REPRESENTATIVE: Gass, David A.; Savereide, Paul B.; Blackburn, Robert P.

NUMBER OF CLAIMS: 17

EXEMPLARY CLAIM: 1

LINE COUNT: 1581

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Damage to cells, tissue and other body parts in a mammalian host may be treated by using a lymphokine or cytotoxin in conjunction with at least one biological modifier, which may be a free radical scavenger or a metabolic inhibitor. The biological modifier is preferably uric acid, buthionine sulphoximine, vitamin C, aspirin, or nordihydroguaiaretic acid. Such a combination may be used to treat, for example, cancer, infectious diseases, and damage caused by radiation therapy, high oxygen tension, and chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 8 OF 13 USPATFULL

ACCESSION NUMBER: 94:1453 USPATFULL

TITLE: Methods of treating tumors with compositions of catecholic butanes

INVENTOR(S): Neiss, Edward S., Denver, CO, United States
Allen, Larry M., Golden, CO, United States
Jordan, Russell T., Fort Collins, CO, United States

PATENT ASSIGNEE(S): Block/Chemex, G.P., Jersey City, NJ, United States (U.S. corporation)

NUMBER DATE

----- -----

PATENT INFORMATION: US 5276060 19940104

APPLICATION INFO.: US 91-685609 19910415 (7)

RELATED APPLN. INFO.: Division of Ser. No. US 87-57481, filed on 3 Jun 1987, now patented, Pat. No. US 5008294 which is a continuation-in-part of Ser. No. US 87-52420,
Searcher : Shears 308-4994

08/882499

filed on 4 May 1987, now abandoned which is a continuation of Ser. No. US 85-699923, filed on 11 Feb 1985, now abandoned which is a continuation-in-part of Ser. No. US 84-578501, filed on 9 Apr 1984, now abandoned which is a continuation-in-part of Ser. No. US 83-465631, filed on 10 Feb 1983, now abandoned which is a continuation-in-part of Ser. No. US 82-365781, filed on 5 Apr 1982, now abandoned which is a continuation-in-part of Ser. No. US 79-49886, filed on 19 Jun 1979, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Rollins, John W.

LEGAL REPRESENTATIVE:

Kenyon & Kenyon

NUMBER OF CLAIMS:

2

EXEMPLARY CLAIM:

1

LINE COUNT:

825

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods useful in the treatment of benign, premalignant and malignant solid tumors, especially those of the skin comprising methods for the administration of pharmacologically active compositions containing catecholic butanes. The invention also relates to methods of preventing the occurrence of tumors, and the use of catecholic butanes as a sunscreening agent. The preferred catecholic butane is nordihydroguaiaretic acid. The preferred methods of application of the compositions containing catecholic butanes are by topical application and intratumor injection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 9 OF 13 USPATFULL

ACCESSION NUMBER: 91:30516 USPATFULL

TITLE: Methods of treating tumors with compositions of catecholic butanes

INVENTOR(S): Neiss, Edward S., Denver, CO, United States

Allen, Larry M., Golden, CO, United States

PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., Denver, CO, United States (U.S. corporation)

NUMBER	DATE
--------	------

PATENT INFORMATION: US 5008294 19910416

APPLICATION INFO.: US 87-57481 19870603 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 87-52120, filed on 4 May 1987, now abandoned which is a continuation of Ser. No. US 85-699923, filed on 11 Feb 1985, now abandoned which is a continuation-in-part of Ser. No. US 84-578501,

Searcher : Shears 308-4994

08/882499

filed on 9 Apr 1984, now abandoned which is a continuation-in-part of Ser. No. US 83-465631, filed on 10 Feb 1983, now abandoned which is a continuation-in-part of Ser. No. US 82-365781, filed on 5 Apr 1982, now abandoned which is a continuation-in-part of Ser. No. US 79-49886, filed on 19 Jun 1979, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Rollins, John W.

LEGAL REPRESENTATIVE:

Kenyon & Kenyon

NUMBER OF CLAIMS:

34

EXEMPLARY CLAIM:

1

LINE COUNT:

983

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods useful in the treatment of benign, premalignant and malignant solid tumors, especially those of the skin comprising methods for the administration of pharmacologically active compositions containing catecholic butanes. The invention also relates to methods of preventing the occurrence of tumors, and the use of catecholic butanes as a sunscreening agent. The preferred catecholic butane is nordihydroguaiaretic acid. The preferred methods of application of the compositions containing catecholic butanes are by topical application and intratumor injection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 10 OF 13 USPATFULL

ACCESSION NUMBER: 91:4937 USPATFULL
TITLE: Therapeutic combination of free-radical scavenger and tumor necrosis factor
INVENTOR(S): Zimmerman, Robert, Lafayette, CA, United States
 Marafino, Jr., Benedict J., San Francisco, CA, United States
PATENT ASSIGNEE(S): Cetus Corporation, Emeryville, CA, United States
 (U.S. corporation)

NUMBER DATE

----- -----

PATENT INFORMATION:

US 4985241 19910115

APPLICATION INFO.:

US 89-399386 19890825 (7)

RELATED APPLN. INFO.:

Continuation of Ser. No. US 87-113643, filed on 26 Oct 1987, now abandoned which is a continuation-in-part of Ser. No. US 86-933475, filed on 21 Nov 1986, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Draper, Garnette D.

LEGAL REPRESENTATIVE:

Giotta, Gregory J.; Hasak, Janet E.; Halluin, Albert P.

Searcher : Shears 308-4994

08/882499

NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 1333

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Damage to cells, tissue and other body parts in a mammalian host may be treated by using a lymphokine or cytotoxin in conjunction with at least one biological modifier, which may be a free radical scavenger or a metabolic inhibitor. The lymphokine or cytotoxin is preferably tumor necrosis factor and the biological modifier is preferably uric acid, buthionine sulphoximine, vitamin C, aspirin, or nordihydroguaiaretic acid. Such a combination may be used to treat, for example, cancer, infectious diseases, and damage caused by radiation therapy, high oxygen tension, and chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 11 OF 13 USPATFULL

ACCESSION NUMBER: 90:5872 USPATFULL
TITLE: Pharmaceutical vehicles for enhancing penetration and retention in the skin
INVENTOR(S): Allen, Larry M., Denver, CO, United States
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., Denver, CO, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4895727	19900123
APPLICATION INFO.:	US 85-730682	19850503 (6)
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Maple, John S.	
LEGAL REPRESENTATIVE:	Kenyon & Kenyon	
NUMBER OF CLAIMS:	30	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	1116	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention is a method of inducing a reservoir effect in skin and mucous membranes so as to enhance penetration and retention and reduce transdermal flux of topically applied therapeutic and cosmetic pharmacologically active agents. The invention also relates to topical treatment methods involving such reservoir effect enhancers, and to pharmaceutical compositions containing them.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 12 OF 13 USPATFULL

ACCESSION NUMBER: 89:92343 USPATFULL
TITLE: Compositions of catecholic butanes with zinc
Searcher : Shears 308-4994

08/882499

INVENTOR(S) : Jordan, Russell T., Fort Collins, CO, United States
PATENT ASSIGNEE(S) : Chemex Pharmaceuticals, Inc., Denver, CO, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4880637	19891114
APPLICATION INFO.:	US 86-924620	19861028 (6)
DISCLAIMER DATE:	20050927	
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 85-699923, filed on 11 Feb 1985, now abandoned which is a continuation-in-part of Ser. No. US 84-578501, filed on 9 Apr 1984, now abandoned which is a continuation-in-part of Ser. No. US 83-465631, filed on 10 Feb 1983, now abandoned which is a continuation-in-part of Ser. No. US 82-365781, filed on 5 Apr 1982, now abandoned which is a continuation-in-part of Ser. No. US 79-49886, filed on 19 Jun 1979, now abandoned	

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Rollins, John W.
LEGAL REPRESENTATIVE: Kenyon & Kenyon
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 1185

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides new compositions comprising catecholic butanes and ionic zinc. The invention also relates to pharmacologically active compositions comprising said new compositions, which are useful in the treatment of benign, premalignant and malignant solid tumors, especially those of the skin. The ionic zinc may be in the form of a zinc salt, and the preferred catecholic butane is nordihydroguaiaretic acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 13 OF 13 USPATFULL
ACCESSION NUMBER: 88:62483 USPATFULL
TITLE: Modification of plant extracts from zygophyllaceae and pharmaceutical use therefor
INVENTOR(S) : Jordan, Russell T., Fort Collins, CO, United States
PATENT ASSIGNEE(S) : Chemex Pharmaceuticals, Inc., Denver, CO, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4774229	19880927
	Searcher :	Shears 308-4994

08/882499

APPLICATION INFO.: US 86-860654 19860507 (6)
RELATED APPLN. INFO.: Continuation of Ser. No. US 82-365784, filed on 5
Apr 1982, now abandoned which is a
continuation-in-part of Ser. No. US 79-49886,
filed on 19 Jun 1979, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Rollins, John
LEGAL REPRESENTATIVE: Kenyon & Kenyon
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
LINE COUNT: 835

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A mixture of an extract from a plant belonging to the
Zygophyllaceae family containing phenolic compositions and a
nonalkali metal salt is useful as a pharmaceutical agent, for
example, in the treatment of cancer, nonmalignant tumors,
osteomyelitis, psoriasis and warts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> fil marpat

FILE 'MARPAT' ENTERED AT 16:54:45 ON 03 JUN 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 1999 American Chemical Society (ACS)

FILE CONTENT: 1988-PRESENT (VOL 108 ISS 12-VOL 130 ISS 22) (19990528/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 5898023 27 APR 1999
DE 19849755 29 APR 1999
EP 913456 06 MAY 1999
JP 11116551 27 APR 1999
WO 9922383 06 MAY 1999

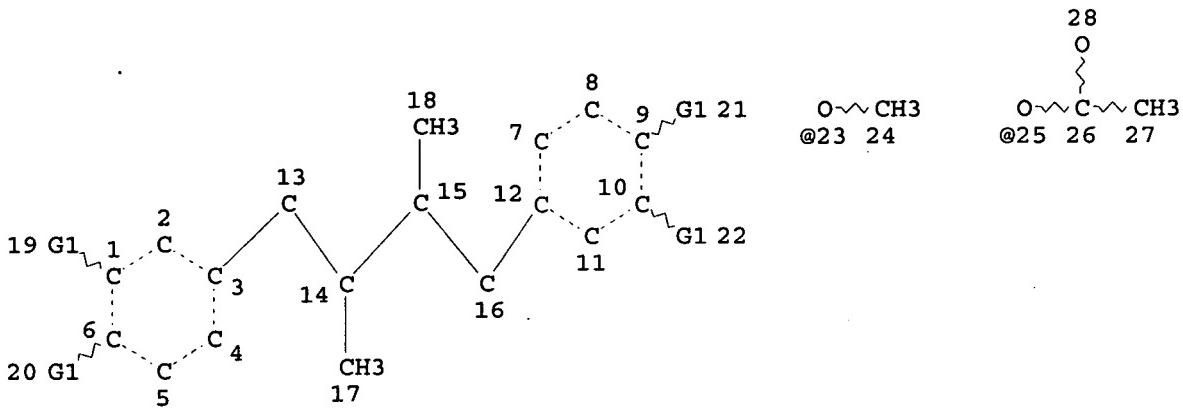
MARPAT structure search limits have been raised.
Enter HELP SLIMIT for details.

=> d que stat

L5 STR

Searcher : Shears 308-4994

08/882499



VAR G1=OH/23/25

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:

ECLEVEL IS LIM ON ALL NODES

ALL RING(S) ARE ISOLATED

L18 17 SEA FILE=MARPAT SSS FUL L5 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 9546 ITERATIONS (1 INCOMPLETE) 17 ANSWERS
SEARCH TIME: 00.01.03

=> d 1-17 .bevmar; fil marpatprev

L18 ANSWER 1 OF 17 MARPAT COPYRIGHT 1999 ACS
(ALL HITs ARE ITERATION INCOMPLETES)

ACCESSION NUMBER: 130:242298 MARPAT

TITLE: Preparation of phthalaldehyde derivatives as antidiabetics

INVENTOR(S): Vertesy, Laszlo; Kurz, Michael; Schindler, Peter; Stump, Heike

PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland GmbH, Germany

SOURCE: Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

Searcher : Shears 308-4994

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 902002	A1	19990317	EP 98-116936	19980908	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
DE 19740080	A1	19990318	DE 97-19740080	19970912	
CA 2246928	AA	19990312	CA 98-2246928	19980911	
				DE 97-19740080	19970912

PRIORITY APPLN. INFO.:

AB Phthalaldehyde derivs., esp. Hericenal C are useful for the treatment of metabolic disorders, esp. glucose metabolic disorders and for the treatment of Diabetes mellitus. Hericenal A, B and C were purified by column chromatog. of cell culture solns. from *Hericium erinaceus*. The effectiveness of the compds. in the inhibition of glucose 6-phosphate translocase was demonstrated for Hericenal, A, B, and C at 8, 8.6, and 8.6 .mu.g/mL.

IC ICM C07C047-544

ICS C07C047-56; A61K031-11

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 1, 26

ST phthalaldehyde deriv antidiabetic; hericenal glucose phosphate translocase inhibition antidiabetic

IT New natural products
(Hericenal A (benzenoid))IT New natural products
(Hericenal B (benzenoid))IT New natural products
(Hericenal C (benzenoid))

IT Glucose transporters

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(glucose phosphate-transporting; prepn. of phthalaldehyde derivs.
as antidiabetics)IT Molecular structure (natural product)
(of Hericenal A (benzenoid))IT Molecular structure (natural product)
(of Hericenal B (benzenoid))IT Molecular structure (natural product)
(of Hericenal C (benzenoid))

IT Antidiabetic agents

Carbohydrate metabolic diseases
Hericium erinaceus

(prepn. of phthalaldehyde derivs. as antidiabetics)

IT 50-99-7, Glucose, biological studies

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU

Searcher : Shears 308-4994

08/882499

(Occurrence); PROC (Process)

(metabolic disorders; prepn. of phthalaldehyde derivs. as
antidiabetics)

IT 483-53-4, Flavipin 643-79-8D, Phthalaldehyde, derivs.
221322-84-5, Hericenal A 221322-87-8, Hericenal B 221322-90-3,
Hericenal C
RL: BAC (Biological activity or effector, except adverse); BOC
(Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(prepn. of phthalaldehyde derivs. as antidiabetics)

L18 ANSWER 2 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 128:290238 MARPAT
TITLE: Use of bisphenolic compounds to treat type II
diabetes

INVENTOR(S): Khandwala, Atul S.; Luo, Jian

PATENT ASSIGNEE(S): Shaman Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

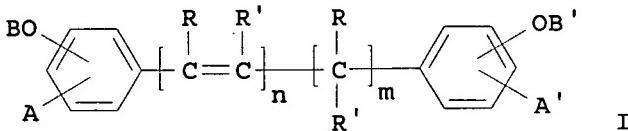
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815266	A1	19980416	WO 97-US18109	19971006
W:	AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5827898	A	19981027	US 96-726591	19961007
AU 9850795	A1	19980505	AU 98-50795	19971006
PRIORITY APPLN. INFO.:			US 96-726591	19961007
			WO 97-US18109	19971006

GI



AB Methods are provided for treatment of non-insulin-dependent diabetes
Searcher : Shears 308-4994

mellitus, for reducing blood glucose levels, or hyperglycemia. The methods entail administering to a mammal in need of such treatment a therapeutically effective amt. of a compn. whose active ingredient consists essentially of a compd. I [R, R' = H, (un)substituted C1-C20 alkyl, (un)substituted C2-C20 alkenyl, or R and R' together form cycloalk(en)yl ring; (C(R):C(R')), (C(R)(R')) are the same or different; A, A' = C2-C20 acylamino, C2-C20 acyloxy, C2-C20 alcanoyle, etc.; B, B' = H, C2-C20 alkanoyl, C3-C20 alkenoyl, C2-C20 alkenyl, etc.; n, m = 0-6] or a pharmaceutically acceptable salt thereof. Also provided are methods of treatment using a bisphenolic compd. in conjunction with another hypoglycemic or hypolipidemic agent. The hypoglycemic activity of nordihydroguaiaretic acid is described.

- IC ICM A61K031-05
 CC 1-10 (Pharmacology)
 ST bisphenolic compd antidiabetic hypoglycemic; nordihydroguaiaretic acid hypoglycemic
 IT Antidiabetic agents
 Glucose transport
 Hypolipemic agents
 (bisphenolic compds. to treat type II diabetes, and combinations with other agents)
 IT Sulfonylureas
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (bisphenolic compds. to treat type II diabetes, and combinations with other agents)
 IT .beta.-Adrenoceptor antagonists
 (.beta.-3-adrenoceptor antagonists; bisphenolic compds. to treat type II diabetes, and combinations with other agents)
 IT 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 500-38-9, Nordihydroguaiaretic acid 504-78-9D, Thiazolidine, derivs. 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 21187-98-4, Gliclazide 27686-84-6 29094-61-9, Glipizide 56180-94-0, Acarbose 72432-03-2, Miglitol 97322-87-7, Troglitazone 103185-28-0 119584-39-3 119584-40-6
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (bisphenolic compds. to treat type II diabetes, and combinations with other agents)
 IT 50-99-7, Glucose, biological studies
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (bisphenolic compds. to treat type II diabetes, and combinations with other agents)
 IT 74315-95-0, .alpha.-Glycosidase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 Searcher : Shears 308-4994

08/882499

(inhibitors; bisphenolic compds. to treat type II diabetes, and combinations with other agents)

L18 ANSWER 3 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 126:211905 MARPAT

TITLE: Preparation of cinnamophilin derivatives as platelet aggregation inhibitors, bronchodilators, antioxidants, and vasodilators

PATENT ASSIGNEE(S): National Science Council, Taiwan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

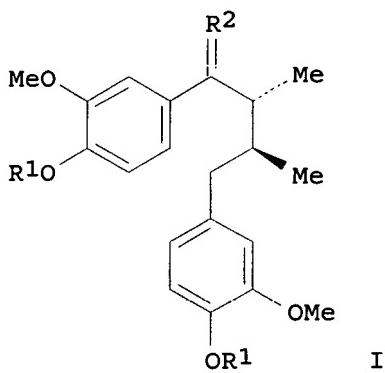
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09040597	A2	19970210	JP 94-336771	19941213

GI



AB The title compds. I [R¹ = H, etc.; R² = O; or C:R² = CHO] are claimed. I [R¹ = H; R² = O] (Cinnamophilin) was isolated from *Cinnamomum philippinense*. Cinnamophilin in vitro showed IC₅₀ of 5.0+-0.4 .mu.M against arachidonic acid-induced platelet aggregation.

IC ICM C07C043-23

ICS A61K031-085; A61K031-12; A61K031-22; A61K031-23; A61K035-78; C07C041-34; C07C049-84; C07C069-16; C09K015-08

CC 25-16 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 11

Searcher : Shears 308-4994

08/882499

ST cinnamophilin isolation Cinnamomum platelet aggregation inhibitor;
Cinnamomum philippinense cinnamophilin isolation; bronchodilator
antioxidant vasodilator cinnamophilin

IT Antioxidants
Bronchodilators
Platelet aggregation inhibitors
Vasodilators
(prepn. of cinnamophilin derivs. as platelet aggregation
inhibitors, bronchodilators, antioxidants, and vasodilators)

IT Cinnamomum philippinense
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of cinnamophilin derivs. as platelet aggregation
inhibitors, bronchodilators, antioxidants, and vasodilators)

IT 154677-96-0P
RL: BAC (Biological activity or effector, except adverse); BOC
(Biological occurrence); PUR (Purification or recovery); THU
(Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP
(Preparation); USES (Uses)
(prepn. of cinnamophilin derivs. as platelet aggregation
inhibitors, bronchodilators, antioxidants, and vasodilators)

IT 156556-85-3P 187939-69-1P 187939-70-4P 187939-71-5P
RL: BAC (Biological activity or effector, except adverse); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)
(prepn. of cinnamophilin derivs. as platelet aggregation
inhibitors, bronchodilators, antioxidants, and vasodilators)

IT 66322-34-7
RL: BOC (Biological occurrence); THU (Therapeutic use); BIOL
(Biological study); OCCU (Occurrence); USES (Uses)
(prepn. of cinnamophilin derivs. as platelet aggregation
inhibitors, bronchodilators, antioxidants, and vasodilators)

IT 108-24-7, Acetic anhydride 334-88-3, Diazomethane
RL: RCT (Reactant)
(prepn. of cinnamophilin derivs. as platelet aggregation
inhibitors, bronchodilators, antioxidants, and vasodilators)

L18 ANSWER 4 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 125:185864 MARPAT

TITLE: Treatment of multidrug-resistant cancers with
nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs

INVENTOR(S): Howell, Stephen; Khandwala, Atul; Sachdev, Om
P.; Smith, Charles G.

PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA

SOURCE: U.S., 15 pp. Cont.-in-part of U.S. 5,409,690.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

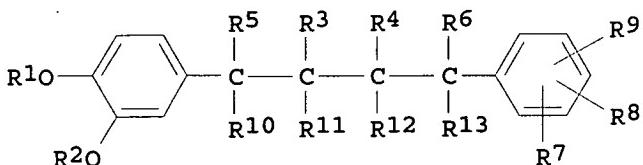
FAMILY ACC. NUM. COUNT: 2

Searcher : Shears 308-4994

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5541232	A	19960730	US 94-264740	19940623
US 5409690	A	19950425	US 93-81663	19930623
PRIORITY APPLN. INFO.:			US 93-81663	19930623

GI



AB A method and compn. for treating multidrug resistance in a mammal are disclosed, in which the compn. includes NDGA (masoprocol) or a NDGA analog I (R1, R2 = H, lower alkyl, lower acyl; R3-R6, R10-R13 = H, lower alkyl; R7-R9 = H, OH, lower alkoxy, lower acyloxy) in a pharmaceutically acceptable vehicle. The method is particularly suitable for administering an antineoplastic agent, and the compn. includes the combination of NDGA, or an analog with such an antineoplastic agent. Activity of NDGA and a topical formulation contg. NDGA are described.

IC ICM A61K031-045

ICS A61K031-05

NCL 514731000

CC 1-6 (Pharmacology)

Section cross-reference(s): 63

ST nordihydroguaiaretate deriv multidrug resistant cancer treatment

IT Acquired immune deficiency syndrome

(cancers in; nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Antibiotics

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Biological transport

Neoplasm inhibitors

Pharmaceutical dosage forms

(nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Coordination compounds

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(platinum-contg.; nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs combined with other
antineoplastic compds., and pharmaceuticals contg. them, for
treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(Hodgkin's disease, nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs, and pharmaceuticals contg.
them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(acute leukemia, nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs, and pharmaceuticals contg.
them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(anus, nordihydroguaiaretic acid and nordihydroguaiaretic acid
analogs, and pharmaceuticals contg. them, for treatment of
multidrug-resistant cancers)

IT Intestine, neoplasm
(anus, inhibitors, nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs, and pharmaceuticals contg.
them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(biliary tract, hepatobiliary; nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs, and pharmaceuticals contg.
them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(bladder carcinoma, nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs, and pharmaceuticals contg.
them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(central nervous system, nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs, and pharmaceuticals contg.
them, for treatment of multidrug-resistant cancers)

IT Nervous system
(central, neoplasm, inhibitors, nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs, and pharmaceuticals contg.
them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(chronic leukemia, nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs, and pharmaceuticals contg.
them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(colon, nordihydroguaiaretic acid and nordihydroguaiaretic acid
analogs, and pharmaceuticals contg. them, for treatment of
multidrug-resistant cancers)

IT Intestine, neoplasm
(colon, inhibitors, nordihydroguaiaretic acid and
nordihydroguaiaretic acid analogs, and pharmaceuticals contg.
them, for treatment of multidrug-resistant cancers)

- IT Pharmaceutical dosage forms
 - (emollients, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (endocrine, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (esophagus, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (female reproductive tract, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Reproductive tract
 - (female, neoplasm, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (head, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Kidney, neoplasm
 - Lung, neoplasm
 - Ovary, neoplasm
 - Pancreas, neoplasm
 - Skin, neoplasm
 - Stomach, neoplasm
 - Testis, neoplasm
 - (inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Pharmaceutical dosage forms
 - (injections, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (kidney, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (leukemia, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Pharmaceutical dosage forms
 - (liposomes, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

Searcher : Shears 308-4994

- multidrug-resistant cancers)
- IT Pharmaceutical dosage forms
 - (liqs., nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (lung, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (lymphocytic lymphoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (lymphoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (mammary gland, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Thorax
 - (mediastinum, neoplasm, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (melanoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (mesothelioma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Drug resistance
 - (multi-, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (neck, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Bladder
 - (neoplasm, carcinoma, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Biliary tract
 - (neoplasm, inhibitors, hepatobiliary; nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

Searcher : Shears 308-4994

- IT Esophagus
- Head
- Mammary gland
- Neck, anatomical
- Penis
- Prostate gland
- Ureter
- Urethra
 - (neoplasm, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Pharmaceutical dosage forms
 - (ointments, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Pharmaceutical dosage forms
 - (ointments, creams, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (osteosarcoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Bone, neoplasm
 - (osteosarcoma, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (ovary, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (pancreas, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (penis, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (plasma-cell myeloma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (prostate gland, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
- IT Neoplasm inhibitors
 - (rectum, nordihydroguaiaretic acid and nordihydroguaiaretic acid

Searcher : Shears 308-4994

analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Intestine, neoplasm
(rectum, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(skin, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(small intestine, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Intestine, neoplasm
(small, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(soft tissue sarcoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Animal tissue
(soft, neoplasm, sarcoma, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(solids, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(stomach, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(testis, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(thorax mediastinum, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(topical, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(transdermal, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

multidrug-resistant cancers)

IT Neoplasm inhibitors
 (ureter, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
 (urethra, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Alkaloids, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (vincleukoblastine, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT 865-21-4, Vinblastine
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT 15663-27-1, Cisplatin 23214-92-8, Doxorubicin
 RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT 7440-06-4D, Platinum, coordination complexes
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT 24150-24-1 27686-84-6 36469-60-0 68930-18-7 101432-05-7
 103185-28-0 119189-27-4 119189-32-1 119189-33-2 119189-34-3
 119189-39-8 119189-40-1 119189-41-2 180634-55-3 180634-56-4
 180634-57-5 180634-58-6 180634-59-7 180634-60-0 180634-61-1
 180634-62-2 180634-63-3 180634-64-4 180634-65-5 180853-56-9
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

L18 ANSWER 5 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER:

125:76343 MARPAT

TITLE:

Nordihydroguaiaretic acid derivatives for the suppression of HIV Tat transactivation

INVENTOR(S):

Huang, Ru Chih; Gnabbe, John N.

PATENT ASSIGNEE(S):

Johns-Hopkins University, USA

Searcher : Shears 308-4994

SOURCE: PCT Int. Appl., 60 pp.
 CODEN: PIXXD2

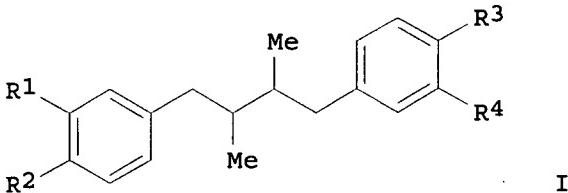
DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610549	A1	19960411	WO 95-US11779	19950922
W: AU, CA, CN, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2200991	AA	19960411	CA 95-2200991	19950922
AU 9536339	A1	19960426	AU 95-36339	19950922
AU 700481	B2	19990107		
EP 783474	A1	19970716	EP 95-933830	19950922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1162301	A	19971015	CN 95-196035	19950922
JP 10509421	T2	19980914	JP 95-511844	19950922
US 5663209	A	19970902	US 96-627588	19960404
PRIORITY APPLN. INFO.:			US 94-316341	19940930
			WO 95-US11779	19950922

GI



AB The invention reveals the isolation, purifn. and characterization from the creosote bush Larrea tridentata of compds. I [R1-R4 = OH, OMe, CH₃C(O)O, provided that R1-R4 are not each OH simultaneously]. Each compd. is a deriv. of 1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane (nordihydroguaiaretic acid, NDGA). In addn., NDGA and each deriv. can be used in a method to suppress Tat transactivation of a lentivirus, including the HIV virus, in a cell by administering NDGA or a deriv. of NDGA to the cell. Fractionation of NDGA derivs. from Larrea tridentata is described. Inhibition of transactivation of HIV promoter activity by NDGA and 4-O-methyl-NDGA was detd.

IC ICM C07C039-12
 ICS A61K035-78; A61K031-045

Searcher : Shears 308-4994

CC 1-5 (Pharmacology)
 Section cross-reference(s) : 63
 ST HIV Tat transactivation inhibition nordihydroguaiaretate deriv;
 lentivirus Tat transactivation inhibition nordihydroguaiaretate
 deriv; Larrea nordihydroguaiaretate deriv Tat transactivation
 inhibition
 IT Creosote bush
 Virucides and Virustats
 (nordihydroguaiaretic acid derivs. from Larrea tridentata for
 suppression of Tat transactivation of HIV or other lentivirus)
 IT Ribonucleic acid formation factors
 RL: BPR (Biological process); BIOL (Biological study); PROC
 (Process)
 (gene tat, nordihydroguaiaretic acid derivs. from Larrea
 tridentata for suppression of Tat transactivation of HIV or other
 lentivirus)
 IT Virus, animal
 (human immunodeficiency, nordihydroguaiaretic acid derivs. from
 Larrea tridentata for suppression of Tat transactivation of HIV
 or other lentivirus)
 IT Virus, animal
 (lenti-, nordihydroguaiaretic acid derivs. from Larrea tridentata
 for suppression of Tat transactivation of HIV or other
 lentivirus)
 IT 500-38-9DP, Nordihydroguaiaretic acid, derivs. 500-38-9P,
 Nordihydroguaiaretic acid 178557-46-5P
 RL: BAC (Biological activity or effector, except adverse); PUR
 (Purification or recovery); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (nordihydroguaiaretic acid derivs. from Larrea tridentata for
 suppression of Tat transactivation of HIV or other lentivirus)
 IT 54473-24-4P 178557-47-6P 178557-48-7P 178557-49-8P
 178557-50-1P 178557-51-2P 178557-52-3P 178557-53-4P
 RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL
 (Biological study); PREP (Preparation); USES (Uses)
 (nordihydroguaiaretic acid derivs. from Larrea tridentata for
 suppression of Tat transactivation of HIV or other lentivirus)

L18 ANSWER 6 OF 17 MARPAT COPYRIGHT 1999 ACS
 ACCESSION NUMBER: 122:42331 MARPAT
 TITLE: Protective layers for optical polarizer films
 INVENTOR(S): Shibue, Toshiaki; Nagayasu, Koichi; Takagi,
 Tosha
 PATENT ASSIGNEE(S): Konishiroku Photo Ind, Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 25 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1

Searcher : Shears 308-4994

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
JP 06118233	A2	19940428	JP 92-271879	19921009		
GI	For diagram(s), see printed CA Issue.					
AB	The films are from cellulose acetate contg. a UV-absorber I and .gtoreq.1 selected from II, III and IV; in I, Y = H, halo, (substituted) alkyl, alkenyl, alkoxy, phenyl; A = H, alkyl, Ph, cycloalkyl, alkylcarbonyl, alkylcarbonyl, alkylsulfonyl, CO(NH)Dn-1; D = alkyl, alkenyl, (substituted) phenyl; n, m = 1, 2; in II, R1,2 = H, alkyl, alkenyl, aryl; R3,4 = halo, alkyl, cycloalkyl, alkenyl, alkoxy, aryl, aryloxy, alkylthio, arylthio, acyl, acylamino, sulfonyl, sulfonamide, OH; m, n = 0-4; in III, R1 = aliph., aryl; Y = non-metal at. group forming 5-8 heterocyclic ring with N; and in IV, R4 = H, alkyl, cycloalkyl, alkenyl, aryl, heterocyclic group, Si(Ra)(Rb)(Rc); Ra Rb, Rc = alkyl, alkenyl, alkoxy, aryl, alkenoxy, aryloxy, R1-3, R5,6 = H, alkyl, cycloalkyl, alkenyl, aryl, acylamino, sulfonamide, alkylamino, alkylthio, arylthio, alkoxy carbonyl, aryloxy carbonyl, halo, OR7; R4 and R5, R5 and R6, and R1 and R6 may form 5-6-member or spiro rings.					
IC	ICM G02B005-30					
	ICS C09K003-00; G02B001-08					
CC	73-11 (Optical, Electron, and Mass Spectroscopy and Other Related Properties)					
ST	polarizer film org protective layer					
IT	Coating materials Polarizers (protective layers for optical polarizer films)					
IT	77-08-7	131-54-4	500-38-9	2985-59-3	4673-51-2	6131-38-0
	10601-04-4	16181-01-4	76460-83-8	82394-21-6	89929-65-7	
	116089-83-9	159946-83-5				
	RL: TEM (Technical or engineered material use); USES (Uses) (protective layers for optical polarizer films)					

L18 ANSWER 7 OF 17 MARPAT COPYRIGHT 1999 ACS
 ACCESSION NUMBER: 120:204700 MARPAT
 TITLE: Positive-type light-senstitive composition
 INVENTOR(S): Yamanaka, Tsukasa; Aoai, Toshiaki; Uenichi,
 Kazuya; Kondo, Shunichi; Kokubo, Tadayoshi
 PATENT ASSIGNEE(S): Fuji Photo Film Co., Ltd., Japan
 SOURCE: Eur. Pat. Appl., 81 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
			Searcher : Shears	308-4994

EP 541112 R: BE, DE, FR, GB JP 06051519	A1 19930512 PRIORITY APPLN. INFO.:	EP 92-119043 JP 92-299093 JP 91-319600 JP 92-47705 JP 92-47782 JP 92-166685 JP 92-299093	19921106 19921013 19911108 19920205 19920205 19920603 19921013
---	---------------------------------------	--	--

AB A pos.-type light-sensitive compn. useful in manuf. of a lithog. plate or a semiconductor device and having less layer shrinkage by baking after exposing, less layer decrease in developing, a good profile, and a high resoln. comprises (a) a resin which is insol. in water and sol. in an alk. aq. soln., (b) a compd. which generates an acid by irradn. with active rays or radial rays, and (c) an acid-decomposable dissoln. inhibitor, having a mol. wt. of not more than 3000 and having groups decomposable by the action of the generated acid to increase the solv. of said inhibitor in an alk. developing soln., wherein said inhibitor (c) is at least one compd. selected from the group consisting of (i) compds. having two of said acid decomposable groups which are sepd. by 10 or more bonded atoms excluding the atoms constituting the acid decomposable groups and (ii) compds. having at least three of said acid decomposable groups and two of said groups which are at the farthest positions are sepd. by 9 or more bonded atoms excluding the atoms constituting the acid decomposable groups.

IC ICM G03F007-004

CC 74-6 (Radiation Chemistry, Photochemistry, and Photographic and Other Reprographic Processes)

ST pos photosensitive compn lithog plate; acid generator pos photosensitive compn

IT Lithographic plates
Semiconductor devices
(manuf. of, pos. photoresist compns. contg. photosensitive acid generators, alkali-sol. resins, and acid-decomposable dissoln. inhibitors for)

IT Phenolic resins, uses
RL: USES (Uses)
(novolak, pos. photoresist compns. contg. photosensitive acid generators, acid-decomposable dessoln. inhibitors and, for lithog. plate and semiconductor device manuf.)

IT Resists
(photo-, pos., contg. photosensitive acid generators, alkali-sol. resins, and acid-decomposable dessoln. inhibitors)

IT 57900-42-2 59626-75-4 62613-15-4 66003-78-9 124737-97-9
142096-70-6 153698-46-5 153698-66-9 153698-67-0
RL: USES (Uses)
(pos. photoresist compn. contg. alkali-sol. resins, acid-decomposable dissoln. inhibitors and, for lithog. plate and Searcher : Shears 308-4994

semiconductor device manuf.)

IT 152238-74-9 153698-48-7 153698-49-8 153698-50-1 153698-51-2
 153698-52-3 153698-53-4 153698-54-5 153698-55-6 153698-56-7
 153698-57-8 153698-58-9 153698-59-0 153698-60-3 153698-61-4
 153698-62-5 153698-63-6 153698-64-7 153698-65-8 153840-05-2
 RL: USES (Uses)
 (pos. photoresist compns. contg. alkali-sol. resins,
 photosensitive acid generators and, for lithog. plate and
 semiconductor device manuf.)

IT 24979-70-2, Poly(p-hydroxystyrene) 27029-76-1 112504-03-7
 123236-78-2
 RL: USES (Uses)
 (pos. photoresist compns. contg. photosensitive acid generators,
 acid-decomposable dessoln. inhibitors and, for lithog. plate and
 semiconductor device manuf.)

IT 153698-58-9P 153698-68-1P 153698-69-2P 153698-70-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and use of, as acid-decomposable dissoln. inhibitor for
 pos. photoresist compns.)

IT 110-87-2, 3,4-Dihydro-2H-pyran 865-47-4 4466-18-6 5292-43-3,
 tert-Butylbromoacetate 24424-99-5, Di-tert-butyldicarbonate
 76937-83-2 110726-28-8 153698-47-6
 RL: RCT (Reactant)
 (reaction of, in prep. acid-decomposable dissoln. inhibitor for
 pos. photoresist compns.)

L18 ANSWER 8 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 119:217422 MARPAT

TITLE: Pharmaceutical compositions containing as active principle associations of vanadium and/or niobium with pyrocatechol derivatives for use in treatment of diabetes and lipid disorders

INVENTOR(S): Maurel, Jean Claude; Kiesgen De Richter, Renaud; Rose, Eric

PATENT ASSIGNEE(S): I.R.2.M., Fr.

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9314751	A1	19930805	WO 93-FR68	19930122
W: CA, JP, RU, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2686512	A1	19930730	FR 92-889	19920128
Searcher : Shears 308-4994				

FR 2686512 B1 19950630

FR 92-889 19920128

- PRIORITY APPLN. INFO.:
- AB The compns. of the invention contain the assocn. of a mol of a deriv. of vanadium or niobium (oxidn. state 4 or 5) with 1-10 mol of a pyrocatechol deriv. (Markush included). The compns. are useful for the treatment of diabetes, hypercholesterolemia, hypertriglyceridemia, hyperlipidemia, and complications assocd. with these disorders. Prepn. of the compds. of the invention (e.g. a niobium-caffeic acid complex) is described, and the hypoglycemic effect of selected compds. was demonstrated in streptozotocin-treated rats.
- IC ICM A61K031-28
ICS A61K033-24
- CC 1-10 (Pharmacology)
- Section cross-reference(s): 63
- ST vanadium pyrocatechol deriv complex antidiabetic; niobium pyrocatechol deriv complex antidiabetic; hypocholesteremic pyrocatechol deriv complex vanadium niobium; hypolipidemic pyrocatechol deriv complex vanadium niobium; hypotriglyceridemic pyrocatechol deriv complex vanadium niobium; caffeic acid niobium complex hypoglycemic
- IT Anticholesteremics and Hypolipemics
Antidiabetics and Hypoglycemics
(pyrocatechol deriv. adducts with derivs. of niobium or vanadium)
- IT Pharmaceutical dosage forms
(injections, of pyrocatechol deriv. adducts with derivs. of niobium or vanadium, for treatment of diabetes or lipid disorder)
- IT Glycerides, biological studies
RL: BIOL (Biological study)
(metabolic disorders, hypertriglyceridemia, treatment of, pyrocatechol deriv. adducts with derivs. of niobium or vanadium for)
- IT Pharmaceutical dosage forms
(oral, of pyrocatechol deriv. adducts with derivs. of niobium or vanadium, for treatment of diabetes or lipid disorder)
- IT Pharmaceutical dosage forms
(tapes, of pyrocatechol deriv. adducts with derivs. of niobium or vanadium, for treatment of diabetes or lipid disorder)
- IT 149-45-1D, Tiron, adducts with derivs. of niobium or vanadium
RL: BIOL (Biological study)
(for treatment of diabetes or lipid disorder)
- IT 55-10-7DP, Vanillomandelic acid, reaction products with sodium orthovanadate 90-05-1DP, Guaiacol, reaction products with niobium tetrachloride-THF 108-55-4DP, Glutaric anhydride, reaction products with dihydroxybenzylamine-HBr and vanadyl sulfate 120-80-9DP, Pyrocatechol, derivs., adducts with derivs. of niobium or vanadium 492-89-7DP, 3-Pentadecylcatechol, reaction products with niobium pentaethoxide 500-38-9DP, Nordihydroguaiaretic acid, reaction products with vanadium oxide 501-16-6DP,

Searcher : Shears 308-4994

trans-3,4-Dihydroxycinnamic acid, reaction products with sodium orthovanadate 530-57-4DP, Syringic acid, reaction products with vanadyl sulfate 1034-01-1DP, Octyl gallate, reaction products with vanadyl sulfate 1314-62-1DP, Vanadium oxide, reaction products with nordihydroguaiaretic acid 3236-82-6DP, Niobium pentaethoxide, reaction products with pentadecylcatechol 7440-03-1DP, Niobium, derivs., adducts with pyrocatechol derivs. 7440-62-2DP, Vanadium, derivs., adducts with pyrocatechol derivs. 10026-12-7DP, Niobium pentachloride, reaction products with dihydroxycinnamic acid 13569-70-5DP, Niobium chloride (NbCl₄), reaction products with guaiacol 13569-70-5DP, Niobium tetrachloride, reaction products with hydroxytyramine acid chloride 13718-26-8DP, Sodium metavanadate, reaction products with dihydroxyphenylalanine sodium salt 13721-39-6DP, Sodium orthovanadate, reaction products with pyrocatechol 21092-95-5DP, reaction products with vanadyl sulfate 27774-13-6DP, reaction products with pyrocatechol. 33491-08-6DP, reaction products with vanadyl sulfate 63302-01-2DP, reaction products with sodium metavanadate 63720-39-8DP, reaction products with glutaric anhydride and vanadyl sulfate 150749-73-8DP, reaction products with vanadyl sulfate 150753-35-8DP, reaction products with vanadyl sulfate 150907-50-9DP, reaction products with vanadyl sulfate

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of diabetes or lipid disorder)

IT 108-55-4, Glutaric anhydride

RL: RCT (Reactant)
(reaction of, with dihydroxybenzylamine-HBr and vanadyl sulfate)

IT 10026-12-7, Niobium pentachloride

RL: RCT (Reactant)
(reaction of, with dihydroxycinnamic acid)

IT 13718-26-8, Sodium metavanadate

RL: RCT (Reactant)
(reaction of, with dihydroxyphenylalanine sodium salt)

IT 63720-39-8, 3,5-Dihydroxybenzylamine hydrobromide

RL: RCT (Reactant)
(reaction of, with glutaric anhydride and vanadyl sulfate)

IT 13569-70-5, Niobium chloride (NbCl₄)

RL: RCT (Reactant)
(reaction of, with guaiacol)

IT 13569-70-5, Niobium tetrachloride

RL: RCT (Reactant)
(reaction of, with hydroxytyramine acid chloride)

IT 492-89-7, 3-Pentadecylcatechol

RL: RCT (Reactant)
(reaction of, with niobium pentaethoxide)

IT 90-05-1, Guaiacol

RL: RCT (Reactant)
(reaction of, with niobium tetrachloride-THF)

IT 1314-62-1, Vanadium oxide, reactions

08/882499

RL: RCT (Reactant)
(reaction of, with nordihydroguaiaretic acid)
IT 3236-82-6, Niobium pentaethoxide
RL: RCT (Reactant)
(reaction of, with pentadecylcatechol)
IT 13721-39-6, Sodium orthovanadate 27774-13-6
RL: RCT (Reactant)
(reaction of, with pyrocatechol)
IT 63302-01-2, 3,4-Dihydroxyphenylalanine sodium salt
RL: RCT (Reactant)
(reaction of, with sodium metavanadate)
IT 55-10-7, Vanillomandelic acid 501-16-6, trans-3,4-Dihydroxycinnamic acid
RL: RCT (Reactant)
(reaction of, with sodium orthovanadate)
IT 500-38-9, Nordihydroguaiaretic acid
RL: RCT (Reactant)
(reaction of, with vanadium oxide)
IT 120-80-9, Pyrocatechol, reactions 530-57-4, Syringic acid
1034-01-1, Octyl gallate 21092-95-5, 3-Benzylxy-4-hydroxyacetophenone 33491-08-6 150749-73-8 150753-35-8
150907-50-9
RL: RCT (Reactant)
(reaction of, with vanadyl sulfate)
IT 9004-10-8, Insulin, biological studies
RL: BIOL (Biological study)
(resistance, treatment of, pyrocatechol deriv. adducts with derivs. of niobium or vanadium for)

L18 ANSWER 9 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 119:105755 MARPAT
TITLE: Silver halide color photographic material
INVENTOR(S): Hirabayashi, Shigeto; Yamazaki, Katsumasa
PATENT ASSIGNEE(S): Konica Co., Japan
SOURCE: Eur. Pat. Appl., 108 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

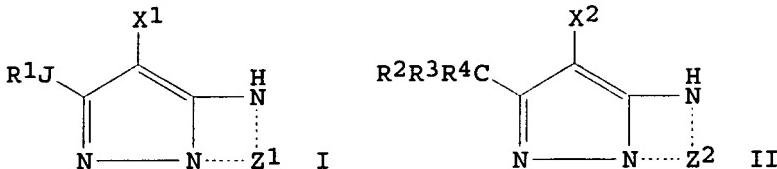
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 515128	A1	19921125	EP 92-304489	19920518
R: DE, FR, GB, NL				
JP 04346341	A2	19921202	JP 91-147905	19910523
JP 04346344	A2	19921202	JP 91-147908	19910523
JP 05100389	A2	19930423	JP 91-292528	19911011
PRIORITY APPLN. INFO.:			JP 91-147905	19910523

Searcher : Shears 308-4994

08/882499

JP 91-147908 19910523
JP 91-292528 19911011

GI



AB A Ag halide color photog. material capable of forming an image of which the characteristic curve ascends with a gentle gradient from the low exposure region to the high exposure region and of forming prints of the same hue irresp. of the type of the printer used comprises 2 kinds of magenta couplers represented by the formulas I and II, resp., (R₁ = H, alkyl, or aryl; R₂₋₄ = H, alkyl, or aryl which may combine with each other to form a satd. or unsatd. ring, provided that .gtoreq.2 of them are not H; J = methylene, O or Si X₁, X₂ = H or a group capable of being released by reaction with an oxidized developing agent; Z₁, Z₂ = a group of nonmetallic atoms necessary for forming a N-contg. heterocyclic ring which may have a substituent).

IC ICM G03C007-30

CC 74-2 (Radiation Chemistry, Photochemistry, and Photographic and Other Reprographic Processes)

ST pyrazolotriazole magenta photog coupler

IT Photographic emulsions
(color, contg. two kinds of magenta dye formers)

IT Photographic couplers
(magenta, pyrazolotriazoles as)

IT 98155-25-0 104660-19-7 104660-32-4 105343-21-3 109870-77-1
110107-47-6 115007-10-8 115311-14-3 115433-13-1 115773-39-2
117661-36-6 124351-77-5 149042-88-6 149042-89-7 149042-90-0
149042-91-1

RL: TEM (Technical or engineered material use); USES (Uses)
(photog. magenta coupler)

L18 ANSWER 10 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 116:15811 MARPAT

TITLE: Methods of treating tumors with compositions of catecholic butanes, their preparation, and use of nordihydroguaiaretic acid for tumor inhibition and as a sunscreen agent

INVENTOR(S): Jordon, Russell T.; Neiss, Edward S.; Allen, Larry M.

PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
Searcher : Shears 308-4994

SOURCE: U.S., 11 pp. Cont.-in-part of U.S. Ser. No.
52,120, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

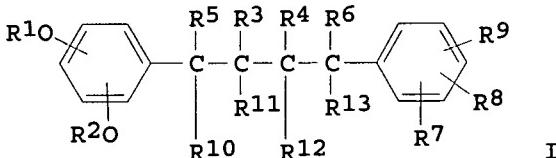
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5008294	A	19910416	US 87-57481	19870603
CA 1334170	A1	19950131	CA 88-568508	19880602
AU 8817360	A1	19881208	AU 88-17360	19880603
EP 297733	A2	19890104	EP 88-305076	19880603
EP 297733	A3	19901205		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8803957	A	19890222	ZA 88-3957	19880603
JP 01079112	A2	19890324	JP 88-135743	19880603
ES 2020011	A6	19910716	ES 88-1751	19880603
US 5276060	A	19940104	US 91-685609	19910415
AU 9220990	A1	19921008	AU 92-20990	19920813
PRIORITY APPLN. INFO.:				
		US 79-49886	19790619	
		US 82-365781	19820405	
		US 83-465631	19830210	
		US 84-578501	19840409	
		US 85-699923	19850211	
		US 87-52120	19870504	
		US 87-52420	19870504	
		US 87-57481	19870603	

GI



AB Catecholic butane derivs. I (R1, R2 = H, lower alkyl, lower acyl, alkylene, R3-R6, R10-R13 = H, lower alkyl; R7-R9 = H, OH, lower alkoxy, lower acyloxy, any 2 adjacent groups together as alkylene dioxo) are provided for treatment of benign, premalignant, and malignant solid tumors, esp. of the skin. Also provided are methods for preventing the occurrence of tumors, and the use of I for sunscreen agents. The preferred I is nordihydroguaiaretic acid (II). Preferred administration methods include topical application and intratumor injection. Prepn. of 1-(3,4-dihydroxyphenyl)-4-

Searcher : Shears 308-4994

(2,3,4-trihydroxyphenyl)butane is described. II was evaluated in a variety of tumor cell lines and in vivo in mice. A methanolic soln. of II absorbed strongly at 2816 .ANG., a sunlight wavelength known to result in sunburn.

IC ICM A61K031-05
 NCL 514731000
 CC 1-6 (Pharmacology)
 Section cross-reference(s): 25, 62
 ST catechol butane deriv antitumor; neoplasm inhibitor catechol butane deriv; sunscreen catechol butane deriv; nordihydroguaiaretic acid antitumor; guaiaretic acid nordihydro antitumor
 IT Neoplasm inhibitors
 (catecholic butane derivs.)
 IT Canis familiaris
 Horse
 (catecholic butane derivs. as tumor inhibitors for)
 IT Sunscreens
 (nondihydroguaiaretic acid for)
 IT Keratosis
 Skin, neoplasm
 (treatment of, catecholic butane derivs. for)
 IT Keratosis
 (actinic, treatment of, catecholic butane derivs. for)
 IT Neoplasm inhibitors
 (adenocarcinoma, catecholic butane derivs. as, for canine breast adenocarcinoma)
 IT Neoplasm inhibitors
 (anus adenoma, catecholic butane derivs. as)
 IT Intestine, neoplasm
 (anus, adenoma, inhibitors, catecholic butane derivs. as)
 IT Neoplasm inhibitors
 (basal cell carcinoma, catecholic butane derivs.)
 IT Skin, neoplasm
 (basal cell carcinoma, inhibitors, catecholic butane derivs.)
 IT Neoplasm inhibitors
 (mast cell carcinoma, catecholic butane derivs.)
 IT Neoplasm inhibitors
 (melanoma, catecholic butane derivs.)
 IT Mammary gland
 (neoplasm, adenocarcinoma, treatment of canine, catecholic butane derivs. for)
 IT Neoplasm inhibitors
 (papilloma, catecholic butane derivs.)
 IT Neoplasm inhibitors
 (sarcoid, catecholic butane derivs.)
 IT Neoplasm inhibitors
 (squamous cell carcinoma, catecholic butane derivs.)
 IT 3929-47-3P 3945-85-5P, 3-(3,4-Dimethoxyphenyl)propyl bromide
 IT 5396-64-5P 81786-49-4P 119189-35-4P 120233-90-1P
 Searcher : Shears 308-4994

08/882499

138172-13-1P 138172-15-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in catecholic butane deriv. tumor
inhibitor prepn.)

IT 119189-34-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for tumor inhibitor)

IT 2103-57-3, 2,3,4-T trimethoxybenzaldehyde 2107-70-2,

3,4-Dimethoxydihydrocinnamic acid

RL: RCT (Reactant)

(reaction of, in catecholic butane deriv. tumor inhibitor prepn.)

IT 500-38-9 5701-82-6 27686-84-6, meso-Nordihydroguaiaretic acid

65987-46-4, 1,4-Bis(3,4-diacetoxyphenyl)-2,3-dimethylbutane

101432-05-7, 1,4-Bis(3,4-dihydroxyphenyl)butane 119189-25-2,

1,4-Bis(3,4-diethoxyphenyl)-2,3-dimethylbutane 119189-26-3,

1,4-Bis(3,4-dipropoxyphenyl)-2,3-dimethylbutane 119189-27-4

119189-28-5 119189-29-6, 1,4-Bis(3,4-dibutyroyloxyphenyl)-2,3-

dimethylbutane 119189-30-9, 1,4-Bis(3,4-divaleroxyloxyphenyl)-2,3-

dimethylbutane 119189-31-0 119189-32-1, 1-(3,4-Dihydroxyphenyl)-

4-phenylbutane 119189-33-2, 1-(3,4-Dihydroxyphenyl)-4-(2,5-

dihydroxyphenyl)butane 119212-35-0 138172-14-2

RL: BIOL (Biological study)

(tumor inhibitor)

IT 500-38-9

RL: BIOL (Biological study)

(tumor inhibitor and sunscreen)

IT 106-97-8D, Butane, catechol derivs. 120-80-9D, Catechol, butane
derivs.

RL: BIOL (Biological study)

(tumor inhibitors)

L18 ANSWER 11 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 114:69042 MARPAT

TITLE: Preparation of lignan compounds as
5-lipoxygenase inhibitors and aldose reductase
inhibitors

INVENTOR(S): Watanabe, Junko; Yanagisawa, Toshihiko; Iketani,
Yukinobu; Mihashi, Hiroshi

PATENT ASSIGNEE(S): Tsumura and Co., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

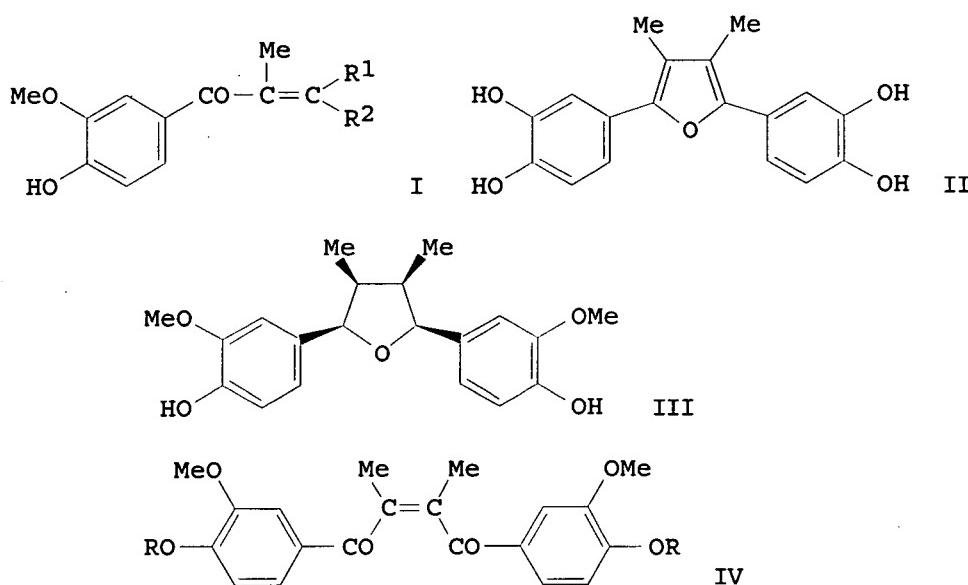
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02180846	A2	19900713	JP 88-335305	19881229
Searcher : Shears 308-4994				

JP 2754644

B2 19980520

GI



AB Lignan compds. I [R1 = Me, R2 = 4,3-HO(MeO)C8H3CO; R1 = 4,3-HO(MeO)C6H3CO, R2 = Me], II, III, etc., are prep'd. for treatment of metab. disorders of arachidonic acid (inflammations, allergy, etc.). Phenolic ketone cis-IV (R = H) (330.7 mg), isolated from Gruaiacum officinale L. resins, was dissolved in DMF and treated with K2CO3 and EtI at room temp. to give 209.2 mg ethered ketone cis-IV (R = Et), which inhibited by 34.6% aldose reductase. The phenolic ketone cis-IV (R = H) showed 99.9% inhibition. Tablet, granular, and injection formulations were given.

ICM C07C049-84

ICS A61K031-12; A61K031-34; C07D307-12; C07D307-42

CC 63-4 (Pharmaceuticals)

Section cross-reference(s) : 1

ST lignan prep'n lipoxygenase inhibitor; aldose reductase inhibitor

lignan prep'n

IT Ligands

RL: PREP (Preparation)

(prep'n. of, as lipoxygenase and aldose reductase inhibitor for treatment of inflammation)

IT 9028-31-3, Aldose reductase 80619-02-9, 5-Lipoxygenase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors, ligand derivs. as, for treatment of metab. disorders

Searcher : Shears 308-4994

08/882499

of arachidonic acid)

IT 131673-01-3
RL: RCT (Reactant)
(isolation and reaction of, in prepn. of lipoxygenase inhibitors
for anti-inflammatory agent)
IT 58096-91-6 131673-02-4 131829-51-1
RL: RCT (Reactant)
(isolation and reaction of, in prepn. of lipoxygenase inhibitors
for inflammation treatment)
IT 4676-33-9P 10035-27-5P 10035-28-6P 58096-85-8P 58096-89-2P
66322-34-7P 74683-16-2P 91377-15-0P 114422-21-8P
131673-03-5P
RL: PREP (Preparation)
(prepn. of, as lipoxygenase and aldose reductase inhibitor for
treatment of inflammation)

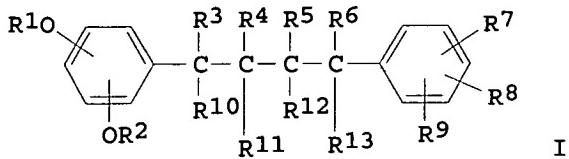
L18 ANSWER 12 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 111:187581 MARPAT
TITLE: Use of catecholic butanes for the treatment of
skin disorders and as neoplasm inhibitors
INVENTOR(S): Neiss, Edward S.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 297733	A2	19890104	EP 88-305076	19880603
EP 297733	A3	19901205	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE	
US 5008294	A	19910416	US 87-57481	19870603
PRIORITY APPLN. INFO.:			US 87-57481	19870603
			US 79-49886	19790619
			US 82-365781	19820405
			US 83-465631	19830210
			US 84-578501	19840409
			US 85-699923	19850211
			US 87-52120	19870504

GI

Searcher : Shears 308-4994



AB A pharmaceutical contains .gtoreq.1 catecholic butanes (I; R1, R2 = H, alkyl, lower acyl, alkylene; R3-R6, R10-R13 = H, alkyl; R7-R9 = H, OH, alkoxy, acyloxy, or any adjacent groups together may be alkyleneoxy). 3,4-Dimethoxydihydrocinnamic acid was esterified to give the Me ester which was reduced to give 3-(3,4-dimethoxyphenyl)propanol. The latter was converted to the mesylate which was converted to 3-(3,4-dimethoxyphenyl)propyl bromide which was converted to the Grignard reagent and treated with 2,3,4-trimethoxybenzaldehyde to give 4-(3,4-dimethoxyphenyl)-1-(2,3,4-trimethoxyphenyl)butanol. This was reduced to give 1-(3,4-dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)butane, which was demethylated with 48% HBr to give 1-(3,4-dihydroxyphenyl)-4-(2,3,4-trihydroxyphenyl)butane. A preferred I is nordihydroguaiaretic acid (meso isomer) (II). Human mammary carcinoma MX-1 was transplanted to mice and treated intratumorally with a compn. contg. 18.40% by wt. II; after 26 days of treatment the wt. of treated tumors was 17.1% of that of nontreated tumors. Using clonogenic (cancer cell) assays II was found to inhibit the growth of canine breast adenocarcinoma tumor cells, MC-1 equine sarcoid cells, and human lung tumor cell line LX-T. II nearly completely prevented tumor promotion by phorbol ester and reduced tumor promotion by dimethylbenzanthrene in mice. I can also be used to treat acne and other skin disorders, or they can be used as sunscreen agents.

IC ICM A61K031-05

ICS A61K031-085; A61K031-22

CC 1-5 (Pharmacology)

Section cross-reference(s): 25

ST catecholic butane neoplasm inhibitor; nordihydroguaiaretic acid skin disease; acne nordihydroguaiaretic acid; sunscreen
nordihydroguaiaretic acid

IT Neoplasm inhibitors
(catecholic butanes)

IT Acne

Skin, disease or disorder
(treatment of, catecholic butanes for)

IT Neoplasm inhibitors
(carcinoma, catecholic butanes)

IT Sunburn and Suntan
(sunscreens, catecholic butanes for)

IT 2103-57-3, 2,3,4-Trimethoxybenzaldehyde

RL: RCT (Reactant)
 (Grignard reaction of, with (dimethoxyphenyl)propyl bromide)

IT 2107-70-2, 3,4-Dimethoxydihydrocinnamic acid

RL: PROC (Process)
 (conversion of, to Me ester)

IT 500-38-9, 1,4-Bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane
 5701-82-6, 1,4-Bis(3,4-dimethoxyphenyl)-2,3-dimethylbutane
 27686-84-6, meso-Nordihydroguaiaretic acid 65987-46-4,
 1,4-Bis(3,4-diacetoxyphenyl)-2,3-dimethylbutane 101432-05-7
 119189-25-2, 1,4-Bis(3,4-diethoxyphenyl)-2,3-dimethylbutane
 119189-26-3, 1,4-Bis(3,4-dipropoxyphenyl)-2,3-dimethylbutane
 119189-27-4 119189-29-6 119189-30-9, 1,4-Bis(3,4-divaleroxyloxyphenyl)-2,3-dimethylbutane 119189-31-0,
 1,4-Bis(3,4-dipivaloyloxyphenyl)-2,3-dimethylbutane 119189-32-1,
 1-(3,4-Dihydroxyphenyl)-4-phenylbutane 119189-33-2,
 1-(3,4-Dihydroxyphenyl)-4-(2,5-dihydroxyphenyl)butane 123292-93-3

RL: BIOL (Biological study)
 (neoplasm inhibitor and antiacne agent and sunscreen agent)

IT 3945-85-5P, 3-(3,4-Dimethoxyphenyl)propyl bromide

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and Grignard reaction of, with trimethoxybenzaldehyde)

IT 81786-49-4P, 3-(3,4-Dimethoxyphenyl)propyl methanesulfonate

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and conversion of, to bromide)

IT 120233-90-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and demethylation of)

IT 27798-73-8P, Methyl 3,4-dimethoxydihydrocinnamate

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and hydride redn. of)

IT 3929-47-3P, 3-(3,4-Dimethoxyphenyl)propanol

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and mesylation of)

IT 119189-35-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and reductive dehydration of)

IT 119189-34-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as neoplasm inhibitor and antiacne agent and sunscreen agent)

L18 ANSWER 13 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 111:17704 MARPAT

TITLE: Neoplasm inhibitors comprising metal salts and phenol derivatives

INVENTOR(S): Jordan, Russell T.; Allen, Larry M.

PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 131 pp.

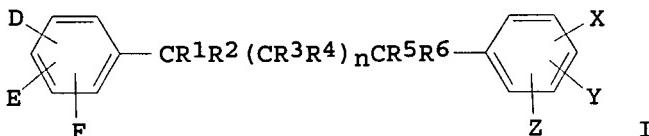
CODEN: PIXXD2

Searcher : Shears 308-4994

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8803805	A1	19880602	WO 86-US2547	19861119
			W: AU, DK, FI, JP, KP, KR, NO, SU RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE	
AU 8767794	A1	19880616	AU 87-67794	19861119
EP 290442	A1	19881117	EP 87-900420	19861119
			R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE	
JP 01501791	T2	19890622	JP 87-500359	19861119
AU 9168662	A1	19910314	AU 91-68662	19910104
PRIORITY APPLN. INFO.:			WO 86-US2547	19861119

GI



AB Antitumor compns. comprise a metal salt and the phenols I [D, E, F, X, Y, Z = H, OH, (un)substituted alkoxy or acyloxy; R1-R6 = H, (un)substituted alkyl or alkoxy, etc.; n = 0, 1-5; the phenolic groups may be joined by CH₂, CH₂CH₂, HOP(O), R₇OP(O); R₇ = alkyl; either of the 2 benzene rings may be replaced by cyclohexyl, naphthyl, tetrahydronaphthyl, pyridyl, piperinyl, quinolinyl, indanyl or indenyl; any R₄-R₆ may be joined with the benzene carbons to form rings]. The metal salts are of Zn, Cr(III), Y, Co(II), Co(III), Ni, Mg, Al, Cu(I), Cu(II), Fe(III), Cd, Sb, Hg, Rb, V, or rare earth metals. 1-(3,4-Dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)butane (prepn. given) was refluxed with HBr under N for 9 h to give 1-(3,4-dihydroxyphenyl)-4-(2,3,4-trihydroxyphenyl)butane (II). Intratumor administration of II together with ZnCl₂ enhanced the survival time and decreased tumor incidence in mice with transplanted human breast adenocarcinoma. An ointment contained ZnCl₂ 10.0, a catecholic butane 5.0, PEG-400 4.2, PEG-8000 61.7, water 19.0 and ascorbic acid 0. mg by wt.

IC ICM A61K033-30
 ICS A61K031-05

CC 1-6 (Pharmacology)

Section cross-reference(s): 25, 27

ST antitumor metal salt phenol deriv; zinc chloride nordihydroguaiaretic
 Searcher : Shears 308-4994

acid antitumor
IT Larrea divaricata
(ext., neoplasm inhibitors contg. metal salts and)
IT Alcohols, biological studies
Aldehydes, biological studies
RL: BIOL (Biological study)
(neoplasm inhibitors contg. metal salts and)
IT Neoplasm inhibitors
(phenolic compd.-metal salt mixts.)
IT Keratosis
(actinic, treatment of, phenolic compd.-metal salt mixt. for)
IT Neoplasm inhibitors
(adenocarcinoma, phenolic compd.-metal salt mixts.)
IT Carboxylic acids, biological studies
RL: BIOL (Biological study)
(aliph., neoplasm inhibitors contg. metal salts and)
IT Skin, neoplasm
(basal cell carcinoma, treatment of, phenolic compd.-metal salt
mixt. for)
IT Intestine, neoplasm
(colon, treatment of, phenolic compd.-metal salt mixt. for)
IT Neoplasm inhibitors
(glioma, phenolic compd.-metal salt mixts.)
IT Bactericides, Disinfectants, and Antiseptics
Fungicides and Fungistats
(medical, phenolic compd.-metal salt mixts.)
IT Neoplasm inhibitors
(melanoma, phenolic compd.-metal salt mixts.)
IT Mast cell
(neoplasm, treatment of, phenolic compd.-metal salt mixt. for)
IT Mammary gland
(neoplasm, adenocarcinoma, treatment of, phenolic compd.-metal
salt mixt. for)
IT Flavonoids
RL: BIOL (Biological study)
(oxo, neoplasm inhibitors contg. metal salts and)
IT Flavonoids
RL: BIOL (Biological study)
(oxo hydroxy, neoplasm inhibitors contg. metal salts and)
IT Flavonoids
RL: BIOL (Biological study)
(oxo hydroxy methoxy, neoplasm inhibitors contg. metal salts and)
IT Neoplasm inhibitors
(renal cell carcinoma, phenolic compd.-metal salt mixts.)
IT Neoplasm inhibitors
(sarcoid, phenolic compd.-metal salt mixts.)
IT Ulcer inhibitors
(skin, phenolic compd.-metal salt mixts.)
IT Neoplasm inhibitors

(squamous cell carcinoma, phenolic compd.-metal salt mixts.)

IT 2103-57-3, 2,3,4-Trimethoxybenzaldehyde
 RL: RCT (Reactant)
 (Grignard reaction of, with dimethoxyphenylpropyl bromide)

IT 1835-04-7, 3,4-Dimethoxypropiophenone
 RL: BIOL (Biological study)
 (condensation of, with bromopropiophenone deriv.)

IT 1835-05-8
 RL: BIOL (Biological study)
 (condensation of, with propiophenone deriv.)

IT 2107-70-2, 3,4-Dimethoxydihydrocinnamic acid
 RL: RCT (Reactant)
 (esterification of, with methanol)

IT 113518-66-4 121160-65-4 121160-66-5 121160-67-6 121160-69-8
 121160-70-1 121160-71-2 121160-73-4 121160-74-5 121160-75-6
 121160-76-7 121160-77-8 121160-78-9 121183-06-0 121202-95-7
 121202-96-8
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (neoplasm inhibitor)

IT 56-53-1D, Diethylstilbestrol, mixts. with metal salts 66-77-3D,
 1-Naphthaldehyde, mixts. with metal salts 66-99-9D,
 2-Naphthaldehyde, mixts. with metal salts 81-64-1D, Quinizarin,
 derivs., mixts. with metal salts 81-64-1D, Quinizarin, mixts. with
 metal salts 88-18-6D, 2-tert-Butylphenol, mixts. with metal salts
 88-89-1D, mixts. with metal salts 89-83-8D, Thymol, mixts. with
 metal salts 90-04-0D, o-Anisidine, mixts. with metal salts
 90-18-6D, Quercetagetin, mixts. with metal salts 90-64-2D,
 Mandelic acid, mixts. with metal salts 91-64-5D, Coumarin,
 derivs., mixts. with metal salts 92-44-4D, 2,3-
 Dihydroxynaphthalene, mixts. with metal salts 95-55-6D,
 2-Aminophenol, mixts. with metal salts 98-29-3D,
 4-tert-Butylcatechol, mixts. with metal salts 98-54-4D,
 4-tert-Butylphenol, mixts. with metal salts 99-50-3D,
 3,4-Dihydroxybenzoic acid, mixts. with metal salts 102-32-9D,
 3,4-Dihydroxyphenylacetic acid, mixts. with metal salts 108-46-3D,
 1,3-Benzenediol, derivs., mixts. with metal salts 108-95-2D,
 Phenol, mixts. with metal salts 110-99-6D, Oxydiacetic acid,
 mixts. with metal salts 112-53-8D, Lauryl alcohol, mixts. with
 metal salts 117-39-5D, Quercetin, mixts. with metal salts
 118-75-2D, mixts. with metal salts 121-33-5D, Vanillin, mixts.
 with metal salts 123-31-9D, 1,4-Benzenediol, mixts. with metal
 salts 123-99-9D, Azelaic acid, mixts. with metal salts
 124-04-9D, Hexanedioic acid, mixts. with metal salts 124-13-0D,
 Octyl aldehyde, mixts. with metal salts 134-01-0D, mixts. with
 metal salts 139-85-5D, 3,4-Dihydroxybenzaldehyde, mixts. with
 metal salts 143-07-7D, Lauric acid, mixts. with metal salts
 153-18-4D, mixts. with metal salts 154-23-4D, mixts. with metal
 salts 303-38-8D, 2,3-Dihydroxybenzoic acid, mixts. with metal

Searcher : Shears 308-4994

salts 315-30-0D, Allopurinol, mixts. with metal salts 331-39-5D,
3,4-Dihydroxycinnamic acid, mixts. with metal salts 437-64-9D,
Apigenin 7-methyl ether, mixts. with metal salts 452-86-8D,
4-Methylcatechol, mixts. with metal salts 476-66-4D, derivs.,
mixts. with metal salts 480-15-9D, Datiscetin, mixts. with metal
salts 480-16-0D, Morin, mixts. with metal salts 480-40-0D,
Chrysin, mixts. with metal salts 482-35-9D, mixts. with metal
salts 491-50-9D, mixts. with metal salts 491-71-4D, Luteolin
3'-methyl ether, mixts. with metal salts 500-38-9D, salts, mixts.
with phenolic compds. 500-66-3D, Olivetol, mixts. with metal salts
504-15-4D, Orcinol, mixts. with metal salts 520-18-3D, Kaempferol,
mixts. with metal salts 526-75-0D, 2,3-Dimethylphenol, mixts. with
metal salts 528-48-3D, Fisetin, mixts. with metal salts
528-53-0D, Delphinidin, mixts. with metal salts 528-58-5D, mixts.
with metal salts 529-44-2D, mixts. with metal salts 529-84-0D,
4-Methyl esculetin, mixts. with metal salts 548-83-4D,
3,5,7-Trihydroxyflavone, mixts. with metal salts 552-54-5D, mixts.
with metal salts 569-77-7D, Purpurogallin, derivs., mixts. with
metal salts 569-77-7D, Purpurogallin, mixts. with metal salts
569-92-6D, Kaempferol 7-methyl ether, mixts. with metal salts
577-85-5D, 3-Hydroxyflavone, mixts. with metal salts 585-34-2D,
3-tert-Butylphenol, mixts. with metal salts 615-94-1D,
2,5-Dihydroxy-p-benzoquinone, mixts. with metal salts 621-82-9D,
Cinnamic acid, mixts. with metal salts 643-84-5D, Enidin, derivs.,
mixts. with metal salts 771-61-9D, Pentafluorophenol, mixts. with
metal salts 970-73-0D, Gallocatechin, mixts. with metal salts
1131-62-0D, mixts. with metal salts 1135-24-6D, mixts. with metal
salts 1143-38-0D, Dithranol, mixts. with metal salts 1154-78-5D,
mixts. with metal salts 1245-15-4D, mixts. with metal salts
1404-00-8D, Mitomycin, mixts. with metal salts 1592-70-7D,
Kaempferol 3-methyl ether, mixts. with metal salts 1696-60-2D,
Vanillin azine, mixts. with metal salts 2068-02-2D, mixts. with
metal salts 2243-27-8D, n-Octyl cyanide, mixts. with metal salts
2896-60-8D, 4-Ethyl resorcinol, mixts. with metal salts
3301-49-3D, Kaempferol 3,7-dimethyl ether, mixts. with metal salts
3943-89-3D, mixts. with metal salts 4382-17-6D, mixts. with metal
salts 4440-92-0D, mixts. with metal salts 4650-71-9D, mixts.
with metal salts 5507-27-7D, mixts. with metal salts 6068-78-6D,
3,3',4'-Trihydroxyflavone, mixts. with metal salts 6068-80-0D,
mixts. with metal salts 6559-91-7D, mixts. with metal salts
6635-20-7D, 5-Nitrovanillin, mixts. with metal salts 7400-08-0D,
p-Hydroxycinnamic acid, mixts. with metal salts 7417-21-2D, mixts.
with metal salts 7429-90-5D, Aluminum, salts, mixts. with phenolic
compds. 7439-89-6D, Iron, salts, mixts. with phenolic compds.
7439-95-4D, Magnesium, salts, mixts. with phenolic compds.
7439-97-6D, Mercury, salts, mixts. with phenolic compds.
7440-02-0D, Nickel, salts, mixts. with phenolic compds.
7440-17-7D, Rubidium, salts, mixts. with phenolic compds.
7440-36-0D, Antimony, salts, mixts. with phenolic compds.

Searcher : Shears 308-4994

7440-43-9D, Cadmium, salts, mixts. with phenolic compds.
7440-47-3D, Chromium, salts, mixts. with phenolic compds.
7440-48-4D, Cobalt, salts, mixts. with phenolic compds.
7440-50-8D, Copper, salts, mixts. with phenolic compds.
7440-62-2D, Vanadium, salts, mixts. with phenolic compds.
7440-65-5D, Yttrium, salts, mixts. with phenolic compds.
7440-66-6D, Zinc, salts, mixts. with phenolic compds. 7646-85-7D,
Zinc chloride (ZnCl₂), mixts. with phenolic compds. 14414-32-5D,
Syringaldazine, mixts. with metal salts 14773-42-3D, mixts. with
metal salts 15663-27-1D, Platinum cis-diaminedichloride, mixts.
with metal salts 16290-26-9D, 3,4-Dihydroxybenzylamine
hydrobromide, mixts. with metal salts 17093-86-6D,
3,3',4',7-Tetramethoxyflavone, mixts. with metal salts
18085-97-7D, 4'-Demethyl eupatilin, mixts. with metal salts
20830-81-3D, Daunomycin, mixts. with metal salts 20869-95-8D,
Kaempferol 3,4'-dimethyl ether, mixts. with metal salts
22368-21-4D, Eupatilin, mixts. with metal salts 23820-56-6D,
mixts. with metal salts 24289-99-4D, mixts. with metal salts
24677-78-9D, mixts. with metal salts 25739-41-7D, Luteolin
7,3'-dimethyl ether, mixts. with metal salts 27554-19-4D,
Kaempferol 3-O-rhamnosylglucoside, mixts. with metal salts
27686-81-3D, mixts. with metal salts 27938-64-3D, mixts. with
metal salts 28281-49-4D, mixts. with metal salts 29289-02-9D,
mixts. with metal salts 29767-20-2D, VM-26, mixts. with metal
salts 33419-42-0D, VP-16, mixts. with metal salts 33708-72-4D,
mixts. with metal salts 36469-60-0D, Dihydroguaiaretic acid,
mixts. with metal salts 40002-23-1D, 3,4-Dihydrobenzoic acid,
mixts. with metal salts 50376-42-6D, Norisoguaiacin, mixts. with
metal salts 51487-58-2D, mixts. with metal salts 54375-47-2D,
Calcein blue, mixts. with metal salts 56305-02-3D, mixts. with
metal salts 65987-46-4D, mixts. with metal salts 68930-19-8D,
mixts. with metal salts 68930-20-1D, mixts. with metal salts
69097-99-0D, mixts. with metal salts 70987-96-1D, mixts. with
metal salts 86788-60-5D, 3,4',5-Trihydroxyflavone, mixts. with
metal salts 94265-62-0D, mixts. with metal salts 100397-63-5D,
mixts. with metal salts 101310-77-4D, mixts. with metal salts
101432-05-7D, glycosides, mixts. with metal salts 101432-05-7D,
mixts. with metal salts 102454-96-6D, mixts. with metal salts
103185-28-0D, mixts. with metal salts 103239-13-0D, mixts. with
metal salts 109202-09-7D, mixts. with metal salts 109202-10-0D,
mixts. with metal salts 109697-15-6D, mixts. with metal salts
110420-30-9D, mixts. with metal salts 119189-27-4D, mixts. with
metal salts 119189-32-1D, 1-(3,4-Dihydroxyphenyl)-4-phenylbutane,
mixts. with metal salts 119189-33-2D, mixts. with metal salts
119189-34-3D, mixts. with metal salts 119189-41-2D, mixts. with
metal salts 119584-35-9D, mixts. with metal salts 119773-32-9D,
mixts. with metal salts 119773-35-2D, mixts. with metal salts
121152-93-0D, mixts. with metal salts 121152-94-1D, mixts. with
metal salts 121152-95-2D, mixts. with metal salts 121152-96-3D,

Searcher : Shears 308-4994

mixts. with metal salts 121152-97-4D, mixts. with metal salts 121152-98-5D, mixts. with metal salts 121152-99-6D, mixts. with metal salts 121153-00-2D, mixts. with metal salts 121153-01-3D, mixts. with metal salts 121153-02-4D, mixts. with metal salts 121153-03-5D, mixts. with metal salts 121153-04-6D, mixts. with metal salts 121209-88-9D, mixts. with metal salts
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (neoplasm inhibitors)

- IT 3945-85-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and Grignard reaction of, with trimethoxybenzaldehyde)
- IT 121153-05-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and Vitride reaction of)
- IT 81786-49-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and bromination of)
- IT 120233-90-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and deetherification of)
- IT 27798-73-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and hydride redn. of)
- IT 119189-35-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and iodination of)
- IT 3929-47-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and mesylation of)

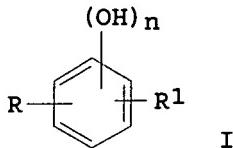
L18 ANSWER 14 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 110:202685 MARPAT
 TITLE: Fogging suppressed silver halide photographic material
 INVENTOR(S): Sakamoto, Hidekazu; Ishige, Osamu
 PATENT ASSIGNEE(S): Konica Co., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63163337	A2	19880706	JP 86-315775	19861225

GI

Searcher : Shears 308-4994



AB In a photog. material comprising .gtoreq.1 Ag halide emulsion layers, the Ag halide emulsion layer and(or) the adjacent hydrophilic colloid layer(s), contains .gtoreq.1 RSm(CS)_nR₁R₂ [R = aryl, 5-6-membered heterocycl; R₁, R₂ = H, aliph., arom.; R₁ and R₂ may join to form a N heterocycle; m = 1, 2; n = 0, 1] and .gtoreq.1 I [n = 2, 3; OH positions are 1,2-, 1,3-, 1,4-, 1,2,3-; R = H, halo, aliph., arom.; R₁ = H, aliph., arom., CO₂H, CO₂M, SO₃H, SO₃M (M = metal), alkoxycarbonyl, COR₂, SO₂R₂, CONHR₃, NHCOR₃ (R₂, R₃ = aliph., arom.]. Fogging during high-temp. development and storage is suppressed.

IC ICM G03C001-34

ICS G03C001-06

CC 74-2 (Radiation Chemistry, Photochemistry, and Photographic and Other Reprographic Processes)

ST fog suppression color film; polyhydroxybenzene fog inhibitor; benzene polyhydroxy fog inhibitor; thiocarbamoyl type fog inhibitor; sulfenamide type fog inhibitor

IT Photographic fog inhibitors
(polyhydroxybenzene and thiocarbamoyl and sulfenamide type)

IT 88-58-4 95-31-8 95-32-9 102-77-2 1166-52-5 2720-65-2
4143-00-4 4568-93-8 24398-42-3 24398-43-4 26773-65-9
29418-16-4 51929-89-6 55605-65-7 60487-86-7 120338-79-6
120338-80-9 120338-81-0 120338-82-1 120338-83-2

RL: USES (Uses)

(photog. fog inhibitors)

L18 ANSWER 15 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 110:179544 MARPAT

TITLE: Drugs for the treatment of skin disorders and tumors containing catecholic butanes and zinc compounds

INVENTOR(S): Jordan, Russell T.; Allen, Larry M.

PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 88 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

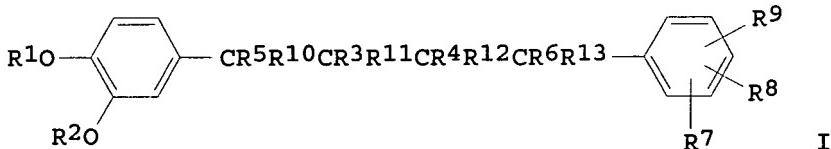
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

08/882499

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8803806	A1	19880602	WO 86-US2549	19861119
		W: AU, DK, FI, JP, KP, KR, NO, SU RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE		
AU 8767379	A1	19880616	AU 87-67379	19861119
PRIORITY APPLN. INFO.:			WO 86-US2549	19861119
GI				



AB Compns. comprising the catecholic butanes I (R1, R2 = H, alkyl, acyl; R3, R4, R5, R6, R10, R11, R12, R13 = H, alkyl; R7, R8, R9 = H, OH, alkoxy, acyloxy) and Zn²⁺ are skin drugs, microbicides and neoplasm inhibitors. 4-(3,4-Dimethoxyphenyl)-1-(2,3,4-trimethoxyphenyl)butanol (prepn. given) was stirred with NaH and MeI in dry DMF, followed by the addn. of H₂O and extn. with CHCl₃, to give an intermediate (not isolated), which upon reaction with Na in liq. NH₃ gave 1-(3,4-dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)butane. This was refluxed with HBr under N for 9 h to give 1-(3,4-dihydroxyphenyl)-4-(2,3,4-trihydroxyphenyl)butane. An ointment comprised ZnCl₂ 10, I 5.0, PEG-400 4.2, PEG-8000 51.7, H₂O 19.0 and ascorbic acid 0.1%. Topical application of a compn. contg. 27.5% ZnCl₂ and 6.9% nordihydroquaiaretic acid reduced the size or completely suppressed B-16 melanoma and sarcoma-180 tumors in mice, and increased the survival time of the animals.

IC ICM A61K033-30

ICS A61K031-05

CC 63-6 (Pharmaceuticals)

Section cross-reference(s) : 25

ST catecholic butane zinc anticancer antimicrobial; phenylbutane prepn drug

IT Propionibacterium acnes

Staphylococcus aureus

(bactericide for, catecholic butane- and zinc-contg. compns.)

IT Bactericides, Disinfectants, and Antiseptics

Fungicides and Fungistats

Neoplasm inhibitors

(catecholic butanes- and zinc-contg. drugs)

IT Wound healing

(stimulation of, by drugs contg. catecholic butanes and zinc)

IT Skin, disease or disorder

Searcher : Shears 308-4994

(treatment of, with catecholic butanes- and zinc-contg. compns.)

IT Acne
 Osteomyelitis
 (treatment of, with catecholic butanes- and zinc-contg. drugs)

IT 2103-57-3, 2,3,4-Trimethoxybenzaldehyde
 RL: RCT (Reactant)
 (Grignard reaction of, with (dimethoxyphenyl)propyl bromide)

IT 500-38-9, Nordihydroguaiaretic acid 546-46-3, Zinc citrate
 553-72-0, Zinc benzoate 557-09-5, Zinc caprylate 557-34-6, Zinc acetate 4468-02-4, Zinc gluconate 7646-85-7, Zinc chloride, biological studies 7699-45-8, Zinc bromide 7733-02-0, Zinc sulfate 7779-88-6, Zinc nitrate 7779-90-0, Zinc phosphate 10139-47-6, Zinc iodide
 RL: BIOL (Biological study)
 (antimicrobial and antineoplastic compn. contg., for skin)

IT 112867-79-5 119189-27-4 119189-32-1 119189-33-2 119189-41-2
 119189-42-3
 RL: BIOL (Biological study)
 (antimicrobial and antineoplastic drug, for skin)

IT 2107-70-2
 RL: RCT (Reactant)
 (esterification of, with methanol)

IT 3945-85-5P
 RL: PREP (Preparation); RCT (Reactant)
 (prepn. and Grignard reaction of, with trimethoxybenzaldehyde)

IT 81786-49-4P
 RL: PREP (Preparation); RCT (Reactant)
 (prepn. and bromination of)

IT 103239-13-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and esterification of)

IT 68930-18-7P 120233-90-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and hydrolysis of)

IT 3929-47-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and mesylation of)

IT 103185-27-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and reaction of)

IT 4440-92-0P 27798-73-8P 119189-35-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and redn. of)

IT 103185-28-0P
 RL: PREP (Preparation)
 (prepn. of, as antimicrobial and antineoplastic drug, for skin)

IT 119189-28-5P 119189-31-0P
 RL: PREP (Preparation)
 (prepn. of, as antimicrobial antineoplastic drug)

08/882499

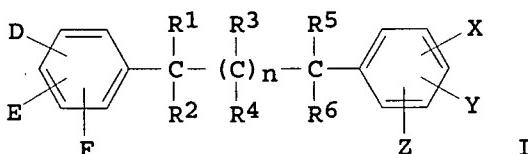
IT 119189-34-3P
RL: PREP (Preparation)
(prepn. of, as antineoplastic drug)
IT 1835-04-7, 3,4-Dimethoxypropiophenone
RL: RCT (Reactant)
(reaction of, with bromodimethoxypropiophenone)
IT 1835-05-8
RL: RCT (Reactant)
(reaction of, with dimethoxypropiophenone)

L18 ANSWER 16 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 110:147880 MARPAT
TITLE: Arachidonic acid lipoxygenase inhibitors for the treatment of psoriasis
INVENTOR(S): Jordan, Russell T.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8803800	A1	19880602	WO 86-US2548	19861119
	W: AU, BB, DK, JP, KP, KR, NO, SU RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE			
AU 8767375	A1	19880616	AU 87-67375	19861119
EP 289506	A1	19881109	EP 87-900421	19861119
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE			
JP 01501790	T2	19890622	JP 87-500248	19861119
AU 9068116	A1	19910314	AU 90-68116	19901217
PRIORITY APPLN. INFO.:			WO 86-US2548	19861119

GI



AB The enzymic action of the arachidonic acid lipoxygenase is inhibited by the administration of diphenylalkyl derivs. (I; D, E, F, X, Y, Z
Searcher : Shears 308-4994

= H, OH, optionally substituted alkoxy or acyl; R1-R6 = lower alkyl, alkoxy, substituted amino, carboxyl, carbalkoxyl, OH, CO, aryl, aralkyl; the Ph rings may contain 1-3 substituents comprising OH, alkenoxy, alkyl, alkoxy, substituted amino, carboxy, carbalkoxy, CF₃, halo, cyano, CH₂OH, SO₃H, sulfonamido, NHSO₂R, NO₂, carbonyloxy, aminocarbonyloxy, aroyloxy, aralkanoyloxy, heteroaryloxy, glycosidylloxy; the phenolic groups may be joined by CH₂, CH₂CH₂, HOPO, alkylOPO, R₂NPO). The 50% inhibiting concn. (IC₅₀) for soybean lipoxygenase by 1-(3,4-dihydroxyphenyl)-4-3,5-diaminophenyl)butane was 1.85 .times. 10⁻⁴ mol/L. For nordihydroguaiaretic acid, a known lipoxidase inhibitor IC₅₀ = 2.9 .times. 10⁻⁴ mol/L. Other compds. tested were e.g. 4-propylcatechol, meso nordihydroguaiaretic acid, and Etoposide; for these IC₅₀ were 4.00, 2.60, 2.10 .times. 10⁻⁴ mol/L, resp.

- IC ICM A61K031-20
 ICS A61K031-075; A61K031-045
 CC 1-12 (Pharmacology)
 ST arachidonic acid lipoxygenase inhibitor psoriasis; catecholic butane psoriasis
 IT Tocopherols
 RL: BIOL (Biological study)
 (arachidonic acid lipoxygenase inhibitor, pharmaceuticals contg., for treatment of psoriasis)
 IT Bronchodilators
 (arachidonic acid lipoxygenase inhibitors)
 IT Uterus
 (contractions, inhibition of, with arachidonic acid lipoxygenase inhibitors)
 IT Hay fever
 Psoriasis
 (treatment of, with arachidonic acid lipoxygenase inhibitors)
 IT Dermatitis
 (allergic, treatment of, with arachidonic acid lipoxygenase inhibitors)
 IT Bronchodilators
 (antiasthmatics, arachidonic acid lipoxygenase inhibitors, catecholic butanes as)
 IT Intestine
 (colon, hpercontraction of, inhibition of, with arachidonic acid lipoxygenase inhibitors)
 IT Eye, disease or disorder
 (conjunctivitis, treatment of, with arachidonic acid lipoxygenase inhibitors)
 IT Digestive tract
 (disease, gastroenteritis, treatment of, with arachidonic acid lipoxygenase inhibitors)
 IT Skin, disease or disorder
 (insect bite, treatment of, with arachidonic acid lipoxygenase inhibitors)

08/882499

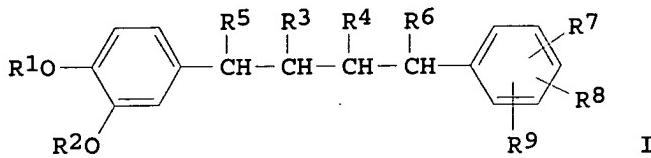
IT 60-10-6, Diphenylthiocarbazone 128-37-0, BHT, biological studies
153-18-4, Rutin 331-39-5, Caffeic acid 500-38-9,
Nordihydroguaiaretic acid 500-38-9D, zinc complexes 518-28-5,
Podophyllotoxin 2525-02-2, 4-Propylcatechol 2896-63-1,
3-Propylcatechol 4375-07-9, Epipodophyllotoxin 5701-82-6
6559-91-7 7440-66-6D, Zinc, NGDA complexes 18085-97-7,
4'-Demethyleupatilin 22368-21-4, Eupatilin 22888-70-6
23077-87-4 27686-84-6 29767-20-2 33419-42-0 40681-80-9
50376-42-6, Norisoguaiacin 56305-04-5, Trolox 59040-30-1,
Nafazatrom 67326-49-2 85129-77-7 86982-61-8 86982-62-9
94265-62-0 119189-27-4 119189-28-5 119189-32-1 119189-33-2
119189-34-3 119584-35-9 119773-32-9 119773-33-0 119773-34-1
119773-35-2 119773-36-3 119789-06-9
RL: BIOL (Biological study)
(arachidonic acid lipoxygenase inhibitor, pharmaceuticals contg.,
for treatment of psoriasis)
IT 63551-74-6, Arachidonic acid lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, catecholic butanes, for treatment of psoriasis)

L18 ANSWER 17 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 110:141554 MARPAT
TITLE: Pharmacologically active compositions of
catecholic butanes with zinc for treatment of
skin diseases
INVENTOR(S): Jordan, Russell T.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8801509	A1	19880310	WO 86-US1740	19860825
W: AU, DK, FI, GB, JP, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8663304	A1	19880324	AU 86-63304	19860825
PRIORITY APPLN. INFO.:			WO 86-US1740	19860825
GI				

Searcher : Shears 308-4994



- AB Catecholic butanes I (R1, R2 = alkyl, acyl; R3, R4 = H, Me, Et; R5, R6 = H, OH; R7, R8, R9 = H, OH, OR1) as Zn salts or chelates, or I mixts. with Zn salts, are drugs for the treatment of skin diseases, esp. fungal or bacterial diseases and cancer. A mixt. of ZnCl₂ 46, meso-1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane 11.5, quercetin 11.5, Na ascorbate 7.7, solvent 3.0, and polyethylene glycol 20.4% by wt., applied topically twice, controlled B-16 melanoma and S-180 tumor, in mice.
- IC ICM A61K033-30
ICS A61K033-24; A61K033-34; A61K033-06; A61K031-05
- CC 63-6 (Pharmaceuticals)
- ST skin drug catechol butane zinc; neoplasm inhibitor skin catechol zinc
- IT Bactericides, Disinfectants, and Antiseptics
Fungicides and Fungistats
Neoplasm inhibitors
(catecholic butane pharmaceuticals contg. zinc as)
- IT Wound healing
(enhancement, catecholic butane pharmaceuticals contg. zinc for)
- IT Larrea divaricata
Rose
(powd., zinc chloride ext., pharmaceuticals contg., for skin disease treatment)
- IT Acne
Osteomyelitis
Skin, disease or disorder
(treatment of, catecholic butane pharmaceuticals contg. zinc for)
- IT 136-53-8 546-46-3, Zinc citrate 553-72-0, Zinc benzoate 557-34-6, Zinc acetate 4468-02-4, Zinc gluconate 7440-66-6D, Zinc, salts and chelates 7646-85-7, Zinc chloride, biological studies 7699-45-8, Zinc bromide 7733-02-0, Zinc sulfate 7779-88-6, Zinc nitrate 7779-90-0, Zinc phosphate 10139-47-6, Zinc iodide
RL: BIOL (Biological study)
(pharmaceuticals contg. catecholic butane derivs. and, for skin disease treatment)
- IT 500-38-9 5701-82-6 27686-84-6 27686-84-6D, D-glucopyranosyl deriv. and its tetraacetate 65987-46-4 101432-05-7 102454-96-6 103185-28-0 113665-39-7 119189-26-3 119189-27-4 119189-28-5 119189-32-1 119189-33-2 119189-34-3 119189-40-1 119584-34-8

Searcher : Shears 308-4994

08/882499

119584-35-9 119584-36-0 119584-37-1 119584-38-2 119584-39-3

119584-40-6 119588-62-4 119607-14-6 119622-63-8

RL: BIOL (Biological study)

(pharmaceuticals contg. zinc salts and, for skin disease
treatment)

FILE 'MARPATPREV' ENTERED AT 16:57:31 ON 03 JUN 1999

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 1999 American Chemical Society (ACS)

FILE COVERS CURRENT RECORDS AND IS UPDATED DAILY

FILE LAST UPDATED: 03 june1999 (19990603/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES

(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 5905069 18 MAY 1999

DE 19823861 29 APR 1999

EP 913729 06 MAY 1999

JP 11124424 11 MAY 1999

WO 9924873 20 MAY 1999

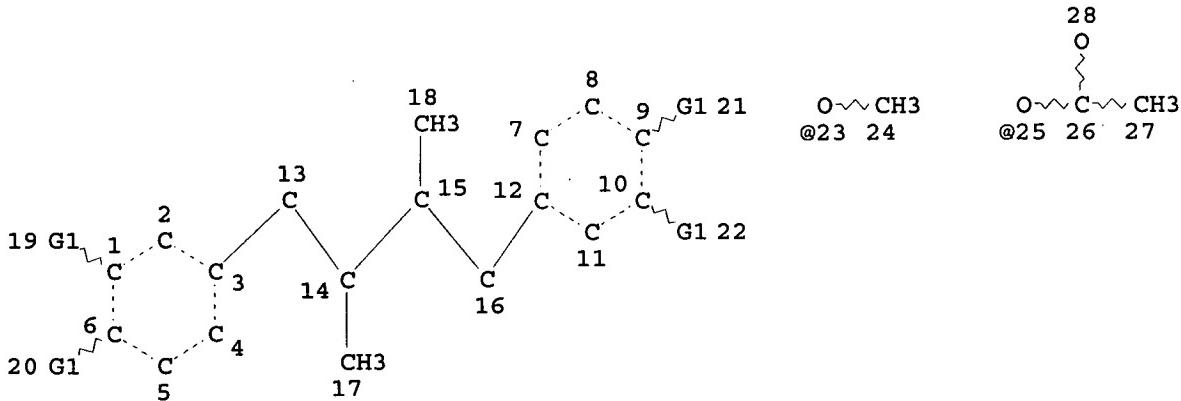
MARPATprev structure search limits have been raised.

Enter HELP SLIMIT for details.

=> d que stat; fil reg

L5

STR



VAR G1=OH/23/25

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

Searcher : Shears 308-4994

08/882499

RSPEC I
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L19 0 SEA FILE=MARPATPREV SSS FUL LS (MODIFIED ATTRIBUTES)

100.0% PROCESSED 67 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.08

FILE 'REGISTRY' ENTERED AT 16:58:16 ON 03 JUN 1999
E "1,4-BIS-(3,4-DIHYDROXYPHENYL)-2,3-DIMETHYLBUTANE"/CN 5

Named Compd.

FILE 'CAPLUS' ENTERED AT 16:58:55 ON 03 JUN 1999
L20 276 SEA ABB=ON PLU=ON BIS(S)(DIHYDROXYPHENYL OR DI(W)(HYDROXYPHENYL OR HYDROXY(W)(PH OR PHENYL)) OR DIHYDROXY(W)(PH OR PHENYL))
L21 3 SEA ABB=ON PLU=ON L20(S)(DIMETHYLBUTANE OR DI(W)(METHYL BUTANE OR (METHYL OR ME)(W) BUTANE) OR DIMETHYL BUTANE)

FILE 'REGISTRY' ENTERED AT 17:00:16 ON 03 JUN 1999
E NDGA/CN 5

L22 1 SEA ABB=ON PLU=ON NDGA/CN

=> d l22 ide can

L22 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1999 ACS
RN 500-38-9 REGISTRY
CN 1,2-BenzeneDiol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Pyrocatechol, 4,4'-(2,3-dimethyltetramethylene)di- (8CI)

OTHER NAMES:

CN .beta.,.gamma.-Dimethyl-.alpha.,.delta.-bis(3,4-dihydroxyphenyl)butane

CN 1,4-Bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane

CN 4,4'-(2,3-Dimethyl-1,4-butanediyl)bis(pyrocatechol)

CN 4,4'-(2,3-Dimethyltetramethylene)dipyrocatechol

CN Butane, 1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethyl-

CN Dihydronorguaiaretic acid

CN Dinorguaiaretic acid, dihydro-

CN NDGA

CN Nordihydroguaiaretic acid

CN Norguaiaretic acid, dihydro-

FS 3D CONCORD

Searcher : Shears 308-4994

08/882499

DR 1413-68-9
MF C18 H22 O4

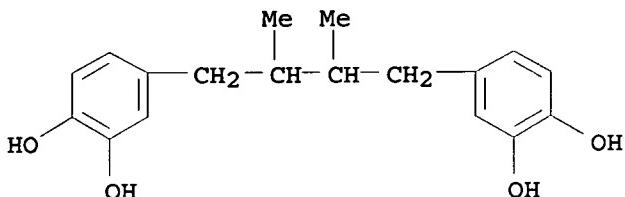
CI COM

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA,
CABA, CANCERLIT, CAOLD, CAPLUS, CEN, CHEMCATS, CHEMLIST, CBNB,
CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB,
IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO,
TOXLINE, TOXLIT, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)



938 REFERENCES IN FILE CA (1967 TO DATE)

11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

938 REFERENCES IN FILE CAPLUS (1967 TO DATE)

17 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:287063

REFERENCE 2: 130:276777

REFERENCE 3: 130:276757

REFERENCE 4: 130:261551

REFERENCE 5: 130:246302

REFERENCE 6: 130:233698

REFERENCE 7: 130:232775

REFERENCE 8: 130:193466

REFERENCE 9: 130:148515

REFERENCE 10: 130:123037

=> d his 123- ful; d 1-8 .bevstr

(FILE 'CAPLUS' ENTERED AT 17:01:24 ON 03 JUN 1999)
Searcher : Shears 308-4994

08/882499

L23 2037 SEA ABB=ON PLU=ON L22 OR NORDIHYDROGUAIARET? OR
NOR(W) (DIHYDROGUAIARET? OR DI(W) (HYDROGUAIARET? OR HYDRO
GUAIARET?)) OR NORDI(W) (HYDROGUAIARET? OR HYDRO GUAIARET?
)
L24 860 SEA ABB=ON PLU=ON NDGA
L25 2264 SEA ABB=ON PLU=ON L23 OR L24
L26 32 SEA ABB=ON PLU=ON L25 AND (VIRAL? OR VIRUS? OR
ANTIVIR? OR HERPES? OR (HSV OR HV)(S)HERPES?)
L27 8 SEA ABB=ON PLU=ON (L21 OR L26) NOT L12

L27 ANSWER 1 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1994:571626 CAPLUS
DOCUMENT NUMBER: 121:171626
TITLE: Expression of porcine leukocyte 12-lipoxygenase
in a baculovirus/insect cell system and its
characterization
AUTHOR(S): Reddy, Ramesh Gala; Yoshimoto, Tanihiro;
Yamamoto, Shozo; Funk, Colin D.; Marnett,
Lawrence J.
CORPORATE SOURCE: Dep. Biochem., Vanderbilt Univ., Nashville, TN,
37232-0146, USA
SOURCE: Arch. Biochem. Biophys. (1994), 312(1), 219-26
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Arachidonate 12-lipoxygenase (12-LO) from porcine leukocytes was expressed in insect cells using a baculovirus expression vector. The recombinant 12-LO was expressed as an N-terminal fusion protein with a 31-amino acid polypeptide carrying a six-histidine tag and an enterokinase cleavage site. Max. intracellular enzyme activity and protein levels were obsd. 48 h after infection of Spodoptera frugiperda cells with the recombinant virus. Cells were lysed and the recombinant protein was purified in a single step by Ni²⁺-nitritilotriacetate column chromatog. The purified enzyme migrated as a single band on sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Recombinant enzyme catalyzed the formation of 12-hydroperoxy-5,8,10,14-eicosatetraenoic acid and a small amt. of 15-hydroperoxy-5,8,11,13-eicosatetraenoic acid. Chiral-phase HPLC anal. indicated that the 12-(S) enantiomer was the predominant product. The purified recombinant 12-lipoxygenase oxygenated linoleic acid to about 19% of the extent of oxygenation of arachidonic acid. Nordihydroguaiaretic acid and 5,8,11,14-eicosatetraynoic acid inhibited the recombinant enzyme with IC₅₀'s of 2.2 and 0.06 .mu.M, resp. Expression of cloned porcine leukocyte 12-LO in S. frugiperda cells and purifn. by Ni²⁺-nitritilotriacetate chromatog. provides a straightforward method for isolation of milligram quantities of this form of 12-LO.

L27 ANSWER 2 OF 8 CAPLUS COPYRIGHT 1999 ACS
Searcher : Shears 308-4994

08/882499

ACCESSION NUMBER: 1993:426488 CAPLUS
DOCUMENT NUMBER: 119:26488
TITLE: Immunomodulation of cellular cytotoxicity to
herpes simplex virus infection
in pregnancy by inhibition of eicosanoid
metabolism
AUTHOR(S): Feinberg, B. B.; Tan, N. S.; Donovan, P. K.;
Loftin, K. C.; Gonik, B.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, USA
SOURCE: J. Reprod. Immunol. (1993), 23(2), 109-18
CODEN: JRIMDR; ISSN: 0165-0378
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In an effort to evaluate the relationships among pregnancy, cellular cytotoxicity and *herpes simplex virus* (HSV) infection, the authors investigated (1) the maternal cellular cytotoxic response to HSV infection as compared with non-pregnant hosts, (2) the influence of both cyclooxygenase and lipoxygenase products on cytotoxicity by selective inhibition of their metabolic pathways, and (3) the potential pregnancy-related differences in immune response to selective inhibition of eicosanoid metab. Indomethacin was used for cyclooxygenase blockade and *nordihydroguaiaretic acid* was used to evaluate lipoxygenase inhibition. In the non-infected animals no differences in cytotoxicity were obsd. between pregnant and non-pregnant groups. HSV infection increased cytotoxicity equally in both groups. Indomethacin did not significantly alter cytotoxicity in either the pregnant or the non-pregnant groups compared with controls. In contrast, NDGA elicited a redn. in the cytotoxic response in both pregnant and non-pregnant hosts. Thus, (1) cytotoxicity is maintained at low levels in the absence of HSV infection, (2) HSV infection induces a significant augmentation in host cellular cytotoxicity, (3) pregnant and non-pregnant cytotoxic responses to HSV infection appear comparable, (4) indomethacin does not augment in vitro cytotoxicity to HSV infection and (5) NDGA suppresses cytotoxicity, providing evidence that lipoxygenase metabolites are essential to cytotoxic cell function.

L27 ANSWER 3 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1989:587581 CAPLUS
DOCUMENT NUMBER: 111:187581
TITLE: Use of catecholic butanes for the treatment of
skin disorders and as neoplasm inhibitors
INVENTOR(S): Neiss, Edward S.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

Searcher : Shears 308-4994

08/882499

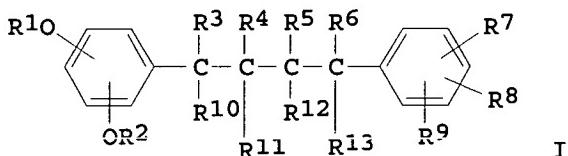
FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 297733	A2	19890104	EP 88-305076	19880603
EP 297733	A3	19901205		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5008294	A	19910416	US 87-57481	19870603
PRIORITY APPLN. INFO.:				
			US 87-57481	19870603
			US 79-49886	19790619
			US 82-365781	19820405
			US 83-465631	19830210
			US 84-578501	19840409
			US 85-699923	19850211
			US 87-52120	19870504

OTHER SOURCE(S): MARPAT 111:187581

GI



AB A pharmaceutical contains .gtoreq.1 catecholic butanes (I; R1, R2 = H, alkyl, lower acyl, alkylene; R3-R6, R10-R13 = H, alkyl; R7-R9 = H, OH, alkoxy, acyloxy, or any adjacent groups together may be alkylenedioxy). 3,4-Dimethoxydihydrocinnamic acid was esterified to give the Me ester which was reduced to give 3-(3,4-dimethoxyphenyl)propanol. The latter was converted to the mesylate which was converted to 3-(3,4-dimethoxyphenyl)propyl bromide which was converted to the Grignard reagent and treated with 2,3,4-trimethoxybenzaldehyde to give 4-(3,4-dimethoxyphenyl)-1-(2,3,4-trimethoxyphenyl)butanol. This was reduced to give 1-(3,4-dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)butane, which was demethylated with 48% HBr to give 1-(3,4-dihydroxyphenyl)-4-(2,3,4-trihydroxyphenyl)butane. A preferred I is nordihydroguaiaretic acid (meso isomer) (II). Human mammary carcinoma MX-1 was transplanted to mice and treated intratumorally with a compn. contg. 18.40% by wt. II; after 26 days of treatment the wt. of treated tumors was 17.1% of that of nontreated tumors. Using clonogenic (cancer cell) assays II was found to inhibit the growth of canine breast adenocarcinoma tumor cells, MC-1 equine sarcoid cells, and human

Searcher : Shears 308-4994

08/882499

lung tumor cell line LX-T. II nearly completely prevented tumor promotion by phorbol ester and reduced tumor promotion by dimethylbenzanthrene in mice. I can also be used to treat acne and other skin disorders, or they can be used as sunscreen agents.

L27 ANSWER 4 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1989:210753 CAPLUS
DOCUMENT NUMBER: 110:210753
TITLE: Reversal of virus-induced alveolar macrophage bactericidal dysfunction by cyclooxygenase inhibition in vitro
AUTHOR(S): Laegreid, W. W.; Liggitt, H. D.; Silflow, R. M.; Evermann, J. R.; Taylor, S. M.; Leid, R. W.
CORPORATE SOURCE: Dep. Vet. Microbiol., Washington State Univ., Pullman, WA, USA
SOURCE: J. Leukocyte Biol. (1989), 45(4), 293-300
CODEN: JLBIE7; ISSN: 0741-5400

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Virus infection of alveolar macrophages (AM) both in vivo and in vitro has been assocd. with a decreased ability of these cells to kill bacteria, together with enhanced prodn. of metabolites of arachidonic acid. These metabolites, esp. PGE2, may be inhibitory to some phagocyte functions. Primary cultures of bovine AM obtained by bronchoalveolar lavage of normal cattle were infected in vitro with parainfluenza-3 (PI3 virus) virus.

Killing of Staphylococcus epidermidis by AM was detd. on days 1-4 post-infection (p.i.). PI3 virus-infected AM killed significantly fewer bacteria on day 4 p.i. compared to uninfected controls (12.1% infected vs. 52.7% controls). Bacterial killing by virus-infected AM, but not control AM, was significantly enhanced on day 4 p.i. by addn. of cyclooxygenase inhibitors 1 h prior to bactericidal assay (28.0% indomethacin, 36.0% mefenamic acid, 38.6% piroxicam, 37.0% NDGA, 44.9% ETYA).

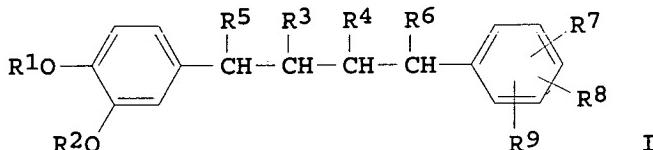
Phagocytosis of opsonized sheep erythrocytes and superoxide generation by virus-infected AM were not significantly increased by cyclooxygenase inhibition. Phagosome-lysosome fusion was severely impaired in virus-infected AM. Pretreatment of virus-infected AM with indomethacin significantly enhanced the percentage of cell expressing fusion activity. Thus, in vitro bactericidal dysfunction assocd. with virus infection of AM is partially the result of enhanced prodn. of prostaglandins or thromboxane by AM and/or an abnormal response to normal levels of endogenously produced cyclooxygenase metabolites. The data further indicate the presence of cyclooxygenase sensitive (phagosome-lysosome fusion) and insensitive (phagocytic) components of virus-induced bactericidal dysfunction in AM.

L27 ANSWER 5 OF 8 CAPLUS COPYRIGHT 1999 ACS
Searcher : Shears 308-4994

08/882499

ACCESSION NUMBER: 1989:141554 CAPLUS
DOCUMENT NUMBER: 110:141554
TITLE: Pharmacologically active compositions of catecholic butanes with zinc for treatment of skin diseases
INVENTOR(S): Jordan, Russell T.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8801509	A1	19880310	WO 86-US1740	19860825
		W: AU, DK, FI, GB, JP, NO RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE		
AU 8663304	A1	19880324	AU 86-63304	19860825
PRIORITY APPLN. INFO.:			WO 86-US1740	19860825
OTHER SOURCE(S):		MARPAT 110:141554		
GI				



AB Catecholic butanes I (R1, R2 = alkyl, acyl; R3, R4 = H, Me, Et; R5, R6 = H, OH; R7, R8, R9 = H, OH, OR1) as Zn salts or chelates, or I mixts. with Zn salts, are drugs for the treatment of skin diseases, esp. fungal or bacterial diseases and cancer. A mixt. of ZnCl₂ 46, meso-1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane 11.5, quercetin 11.5, Na ascorbate 7.7, solvent 3.0, and polyethylene glycol 20.4% by wt., applied topically twice, controlled B-16 melanoma and S-180 tumor, in mice.

L27 ANSWER 6 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1985:540026 CAPLUS
DOCUMENT NUMBER: 103:140026
TITLE: Inhibitors of fatty acid metabolism prevent development of interferon inducing capacity in "aging" chick embryo cells
AUTHOR(S): Sekellick, Margaret J.; Marcus, Philip I.
Searcher : Shears 308-4994

CORPORATE SOURCE: Microbiol. Sect., Univ. Connecticut, Storrs, CT,
06268, USA
 SOURCE: Biol. Interferon Syst. Proc. TNO-ISIR Meet.
 (1985), Meeting Date 1984, 183-7. Editor(s):
 Kirchner, Holger; Schellekens, Huub. Elsevier:
 Amsterdam, Neth.
 CODEN: 54CNA6
 DOCUMENT TYPE: Conference
 LANGUAGE: English
 AB An interferon inducible state was acquired in primary chick embryo cells as they aged in vitro in the presence of Newcastle disease virus. The interferon inducing capacity was prevented by addn. of indomethacin, which inhibited the synthesis of C20 oxygenated fatty acids by blocking the action of fatty acid cyclooxygenase. Other drugs, ibuprofen, aspirin, naproxene, and **nordihydroguaiaretic acid**, which inhibit the synthesis of prostaglandins or leukotrienes also prevented development of interferon inducibility.

L27 ANSWER 7 OF 8 CAPLUS COPYRIGHT 1999 ACS
 ACCESSION NUMBER: 1985:452608 CAPLUS
 DOCUMENT NUMBER: 103:52608
 TITLE: Products of the lipoxygenase pathway in human natural killer cell cytotoxicity
 AUTHOR(S): Rossi, Paolo; Lindgren, Jan Aake; Kullman, Charlotte; Jondal, Mikael
 CORPORATE SOURCE: Dep. Immunol., Karolinska Inst., Stockholm, S-104 01, Swed.
 SOURCE: Cell. Immunol. (1985), 93(1), 1-8
 CODEN: CLIMB8; ISSN: 0008-8749
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB As earlier data suggested the importance of lipoxygenase activation for expression of human natural killer (NK) cell cytotoxicity, 4 different lipoxygenase inhibitors were tested for suppression of NK cell lysis. All inhibitors were active at nontoxic concns., with 50% inhibition at .apprx.15 .mu.M for **nordihydroguaiaretic acid (NDGA)**. NK cell lysis could be reconstituted in NDGA-suppressed cells with leukotriene B4 (LTB4), the all-trans isomers 6-trans-LTB4 and 12-epi-6-trans-LTB4, and 20-carboxyl-LTB4. LTB4 reconstitution was best in the concn. range 1-100 pM and was near control levels at both higher and lower concns. **Herpesvirus Ateles**-transformed killer T cells could also be inhibited by NDGA. Lipoxygenase activity is apparently required for human NK cell lysis, and several different LTB4-related products can restore NK activity in inhibited cells; probably the lipoxygenase pathway is present in the killer cell population.

08/882499

L27 ANSWER 8 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1983:437026 CAPLUS
DOCUMENT NUMBER: 99:37026
TITLE: Leukotriene B4 augments human natural cytotoxic cell activity
AUTHOR(S): Rola-Pleszczynski, Marek; Gagnon, Lyne; Sirois, Pierre
CORPORATE SOURCE: Fac. Med., Univ. Sherbrooke, PQ, J1H 5N4, Can.
SOURCE: Biochem. Biophys. Res. Commun. (1983), 113(2), 531-7
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leukotriene B4 (LTB4) augments human natural cytotoxic lymphocyte activity against target cells infected with *herpes simplex virus*. This activity is partially inhibited by the lipoxygenase inhibitor *nordihydroguaiaretic acid* and the thromboxane synthetase inhibitor OKY-1581, but is augmented by the prostaglandin synthesis inhibitor, indomethacin. Thus, LTB4 may play a role in early host defense responses during inflammatory and infectious disease processes.

=> d his l28- ful; d 1-70 ibib abs

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGB, DRUGNL, DRUGLAUNCH, AIDSLINE' ENTERED AT 17:05:19 ON 03 JUN 1999)

L28 6 SEA ABB=ON PLU=ON L21
L29 9584 SEA ABB=ON PLU=ON L23
L30 3981 SEA ABB=ON PLU=ON L24
L31 151 SEA ABB=ON PLU=ON (L29 OR L30) AND (VIRAL? OR VIRUS?
OR ANTIVIR? OR HERPES? OR (HSV OR HV) (S) HERPES?)
L32 156 SEA ABB=ON PLU=ON L28 OR L31
L33 78 DUP REM L32 (78 DUPLICATES REMOVED)
L34 17 SEA ABB=ON PLU=ON L31 AND ADMIN?
L35 137 SEA ABB=ON PLU=ON L31 AND (SUPPRESS? OR INHIBIT? OR
TREAT? OR THERAP? OR PREVENT?)
L36 143 SEA ABB=ON PLU=ON L28 OR L34 OR L35
L37 70 DUP REM L36 (73 DUPLICATES REMOVED)

L37 ANSWER 1 OF 70 TOXLIT
ACCESSION NUMBER: 1999:14060 TOXLIT
DOCUMENT NUMBER: CA-130-276777U
TITLE: Nontoxic extract of *Larrea tridentata*, production method, and therapeutic use.
AUTHOR: Sinnott RA
SOURCE: (1999). PCT Int. Appl. PATENT NO. 9917609 04/15/1999
(Larreacorp, Ltd.).
CODEN: PIXXD2.

Searcher : Shears 308-4994

PUB. COUNTRY: UNITED STATES
 DOCUMENT TYPE: Patent
 FILE SEGMENT: CA
 LANGUAGE: English
 OTHER SOURCE: CA 130:276777
 ENTRY MONTH: 199905

AB A nontoxic, therapeutic agent having pharmacol. activity comprising concd. ext. of *Larrea tridentata* plant material and ascorbic acid is made by a process in which the plant material is extd. using an org. solvent, and is then satd. with ascorbic acid to reduce the toxic NDGA quinone, which naturally occurs in the plant material, to NDGA itself. Addnl. amts. of ascorbic acid are added to the ext. to inhibit the natural oxidn. of the NDGA into the toxic NDGA quinone in vivo, or during processing or storage. The resulting ext. is useful in the treatment of viral diseases caused by viruses from the *Herpesviridae* family or viruses which require the Sp1 class of proteins to initiate viral replications. The resulting compd. can also be used as an antiinflammatory when the inflammatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize NDGA as a therapeutic agent or a food additive.

L37 ANSWER 2 OF 70 AIDSLINE

ACCESSION NUMBER: 1998:17463 AIDSLINE
 DOCUMENT NUMBER: ICA12-98393903
 TITLE: Involvement of chemokine receptors in the induction of interferon by HIV-1.
 AUTHOR: Capobianchi M R
 CORPORATE SOURCE: Institute For Virology, Rome, Italy.
 SOURCE: Int Conf AIDS, (1998). Vol. 12, pp. 273 (Abstract No. 21172).

PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: (MEETING ABSTRACTS)
 FILE SEGMENT: ICA12
 LANGUAGE: English
 ENTRY MONTH: 199812

AB BACKGROUND: Persistent activation of the interferon (IFN) system underlies progressing HIV infection. HIV, through its external glycoprotein, induces IFN alpha and gamma in normal PBMC, as a consequence of interaction with both CD4 and galactocerebroside. Additionally, chemokine receptors are involved in HIV infection, mediating virus envelope fusion with the target cells. The study was aimed to explore the involvement of chemokine receptors in IFN induction by HIV-1. METHODS: Fixed HIV-1-infected cells were used as IFN inducer in normal PBMC cultures. Newcastle disease virus (NDV) was used as conventional virus inducer of IFN alpha. Chemokines were used as competitors, and MAbs or

Searcher : Shears 308-4994

polyclonal antibodies were used as inhibitors of membrane interactions involved in IFN induction. Methabolic inhibitors were used to block specific signal transduction pathways, either directly or indirectly bound to the chemokine receptor signaling. RESULTS: The alpha-chemokine SDF-1 beta, known to block the infection of T-tropic HIV strains due to interaction with the chemokine receptor CXCR4, inhibits IFN induction by HIV-1 IIIB (a T-tropic strain). On the contrary, the beta-chemokines RANTES, MIP1-alpha and -beta, recognizing CCR5, necessary for the infection by moncytotropic HIV, are virtually ineffective in the IFN induction by HIV-1 IIIB. Furthermore, the MAb 12G5, and polyclonal antibodies, both recognizing CXCR4, dose-dependently inhibit IFN induction by HIV IIIB, and not by NDV. The inhibitor of the protein-tyrosin kinase pathway HA, but not PTX, i.e. an inhibitor of trimeric G-protein activation, inhibits IFN induction by HIV-infected cells. Furthermore, both the cyclooxygenase inhibitor Indo-M, and the lipoxygenase inhibitor NDGA, involved in the arachidonate metabolism, are virtually ineffective in IFN induction by HIV. CONCLUSIONS: These results suggest that HIV-1 induces IFN production through unconventional pathways. In fact, the interaction of gp120 with the appropriate chemokine receptor is required, besides CD4 binding, in order to obtain efficient IFN induction by HIV. Furthermore, chemokine receptor driven signal transduction pathway, such as protein-tyrosine kinase activation, seems to be required, while trimeric G-protein activation and arachidonate metabolism seem not to be involved.

L37 ANSWER 3 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1998-261002 [23] WPIDS
 CROSS REFERENCE: 99-023379 [02]
 DOC. NO. CPI: C98-080992
 TITLE: Extract of Larrea tridentata with reduced NGDA
 quinone levels - useful as anti-viral
 and anti-inflammatory agent.
 DERWENT CLASS: B04 D13
 INVENTOR(S): CLARK, D W; DEBOER, K F; SINNOTT, R A
 PATENT ASSIGNEE(S): (LARR-N) LARREACORP LTD
 COUNTRY COUNT: 68
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9815184	A1	980416	(9823)*	EN	23
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					

Searcher : Shears 308-4994

08/882499

AU 9748956 A 980505 (9836)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9815184	A1	WO 97-US18103	971007
AU 9748956	A	AU 97-48956	971007

FILING DETAILS:

PATENT NO	KIND	PATENT NO
-----	-----	-----
AU 9748956	A Based on	WO 9815184

PRIORITY APPLN. INFO: US 96-726686 961007

AN 1998-261002 [23] WPIDS

CR 99-023379 [02]

AB WO 9815184 A UPAB: 19990113

Method of preparing a non-toxic extract of *Larrea tridentata* plant material involves: (a) extracting the plant material with a solvent to produce an extract containing NDGA (nordihydroguaiaretic acid) quinone; (b) filtering the extract; (c) adding an emulsifying and stabilising agent to the extract; (d) reducing the NDGA quinone with a compound Q; Q = ascorbic acid (or ester or salt), butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulphide, hypophosphorous acid monothioglycerol, potassium bisulphite, propyl gallate, sodium bisulphite, sodium hydrosulphite, sodium thiosulphite, sulphur dioxide, sulphurous acid, a tocopherol or vitamin E. Also claimed are pharmaceutical preparations (i) containing NDGA and/or Mal.4 (3-O-methyl-NDGA) obtained by the above method or (ii) containing NDGA and a compound Q.

USE - NDGA and Mal.4 are recognised as having therapeutic value as anti-viral, and anti-inflammatory and anti-cancer agents. Use of extracts of *Larrea tridentata* for treatment has been hampered by the presence of toxic amounts of the NDGA quinone in previous preparations. The extracts are also useful as non-toxic food additives to prevent oxidation and spoilage.

ADVANTAGE - This method reduces any quinone present and by using additional reducing agents after preparation protects against re-oxidation on storage.

Dwg.0/0

L37 ANSWER 4 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1999-023379 [02] WPIDS

CROSS REFERENCE: 98-261002 [23]

DOC. NO. CPI: C99-007033

Searcher : Shears 308-4994

08/882499

TITLE: Preparing a composition comprising an extract of Larrea tridentata - extracting Larrea tridentata plant material with acetone, reducing NDGA quinone to NDGA using ascorbic acid, and concentrating extract.

DERWENT CLASS: B04 D13

INVENTOR(S): CLARK, W D; DEBOER, K F; SINNOTT, R A

PATENT ASSIGNEE(S): (LARR-N) LARREACORP LTD

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5837252	A	981117 (9902)*			11

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5837252	A Provisional	US 96-20946	960701
		US 96-726686	961007

PRIORITY APPLN. INFO: US 96-20946 960701; US 96-726686 961007

AN 1999-023379 [02] WPIDS

CR 98-261002 [23]

AB US 5837252 A UPAB: 19990113

Preparing a composition comprising an extract of Larrea tridentata comprises; (a) harvesting leaves from Larrea tridentata shrubs; (b) air drying the leaves at ambient temperature and humidity for at least 1 week; (c) maintaining the plant material in whole form; (d) extracting the Larrea tridentata extract by recirculating acetone over the plant material at least 3 times to give a Larrea tridentata extract that contains nordihydroguaiaretic acid quinone (NDGA quinone); (e) filtering particulate impurities from the extract; adding polysorbate 80 (5 ml) to the extract (50 l) as an emulsifying and stabilising agent; (f) reducing the NDGA quinone in the extract to NGDA by passing the extract through a column packed with powdered ascorbic acid (5 g ascorbic acid per litre of extract) to reduce the extract; (g) concentrating the reduced extract by 90% by boiling off the reduced acetone solvent at 100 deg. C; (h) adding additional ascorbic acid to prevent oxidation of the NDGA; and (i) optionally combining the concentrated abstract with carriers, excipients and/or agents.

USE - The extract has anti-inflammatory and antiviral activity, e.g. against Hepes (all claimed), particularly against Hepes simplex type 1 (HSV-1), and Kaposi's Sarcoma.

Administration is topical, formulated as a lotion, or encapsulated.

Searcher : Shears 308-4994

08/882499

ADVANTAGE - The preparation of the extract minimises the oxidation of NDGA to NDGA which is toxic.

Dwg. 0/5

L37 ANSWER 5 OF 70 TOXLIT
ACCESSION NUMBER: 1998:67471 TOXLIT
DOCUMENT NUMBER: CA-128-275069M
TITLE: Nontoxic therapeutic extract of *Larrea tridentata*.
AUTHOR: Sinnott RA; Clark DW; De Boer KF
SOURCE: (1998). PCT Int. Appl. PATENT NO. 9815184 04/16/1998
(De Boer, Kenneth Frank).
CODEN: PIXXD2.
PUB. COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 128:275069
ENTRY MONTH: 199805

AB A nontoxic, therapeutic agent having pharmacol. activity comprising concd. ext. of *Larrea tridentata* and a reducing agent, such as ascorbic acid, an ascorbic acid ester, an ascorbic acid salt, butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulfide, hypophosphorous acid, monothioglycerol, potassium bisulfite, Pr gallate, sodium bisulfite, sodium hydrosulfite, sodium thiosulfate, sulfur dioxide, sulfurous acid, a tocopherol, or vitamin E. The active principle is **nordihydroguaiaretic acid (NDGA)**. The plant material is extd. using an org. solvent, preferably acetone, and is then satd. with one of the listed reducing agents to reduce the toxic NDGA quinone, which naturally occurs in the plant material, to NDGA itself. Addnl. amts. of reducing agent may be added to the ext. to inhibit the natural oxidn. of the NDGA into the toxic NDGA quinone in vivo, or during processing or storage. The resulting ext. is useful in the treatment of viral diseases caused by viruses from the *Herpesviridae* family or viruses which require the Sp1 class of proteins to initiate viral replications. The resulting compd. can also be used as an anti-inflammatory agent when the inflammatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize NDGA as a therapeutic agent or a food additive.

L37 ANSWER 6 OF 70 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998350158 MEDLINE
DOCUMENT NUMBER: 98350158
TITLE: Antiviral activities of methylated
nordihydroguaiaretic acids. 2. Targeting
Searcher : Shears 308-4994

**herpes simplex virus replication by
the mutation insensitive transcription
inhibitor tetra-O-methyl-NDGA.**

AUTHOR: Chen H; Teng L; Li J N; Park R; Mold D E; Gnabre J;
Hwu J R; Tseng W N; Huang R C

CORPORATE SOURCE: Institute of Medicinal Biotechnology, Chinese Academy
of Medical Sciences, Beijing, China, Organosilicon
and Synthesis Laboratory, Department of Chemistry,
National Tsing Hua University, Hsinchu, China-Taiwan.

CONTRACT NUMBER: 1 RO1 DE12165 (NIDR)

SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (1998 Jul 30) 41 (16)
3001-7.
Journal code: J0F. ISSN: 0022-2623.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199810

ENTRY WEEK: 19981004

AB We had previously reported that tetramethyl-O-NGDA (M4N), a synthetic derivative of the naturally occurring nordihydroguaiaretic acid (NDGA), is able to inhibit HIV Tat transactivation by blocking host Sp1 protein at the Sp1 cognate binding site on the HIV LTR promoter. The present studies were undertaken to examine whether M4N is able to inhibit the replication of herpes simplex virus (HSV), another Sp1-regulated virus. The results showed that in Vero cells, M4N inhibits at micromolar levels ($IC_{50} = 43.5 \text{ microM}$) the expression of the herpes immediate early gene (alpha-ICP4), which is essential for HSV replication. An electrophoretic mobility shift assay, examining Sp1 binding to the alpha-ICP4 promoter, showed a significant inhibition of the control bands: 88% inhibition of the fast moving band (FMB) and 45% of the slow moving band (SMB), at 100 μM of drug concentration. Comparative studies between M4N and acycloguanosine (acyclovir, ACV) in cultured Vero cells revealed an interesting pattern in the drug sensitivity (IC_{50}) and cytotoxicity (TC_{50}) parameters. For M4N, the IC_{50} varied between 11.7 and 4 μM in 10 passages of HSV-1 and 4 passages of HSV-2 with no indication for a requirement of higher drug concentration. In contrast, for acyclovir, the IC_{50} increased from 7 μM in the first passage to 444 μM in the tenth passage of HSV-1, and >88 μM for the fourth passage of HSV-2, indicating a rapid build-up of drug resistance against acyclovir. While the selective index (SI), defined as the ratio: TC_{50}/IC_{50} , remained relatively constant for M4N; it dropped 60-fold for acyclovir in the endpoints of viral passages. Drug sensitivity for M4N toward the acyclovir-sensitive strain (sm44) and the acyclovir-resistant strain

Searcher : Shears 308-4994

08/882499

(ACV-10) of HSV-1 was similar, indicating no cross-resistance between M4N and acyclovir in their anti-HSV effects. These results may have an important clinical relevance since HSV has been shown to be a factor for spreading of HIV.

L37 ANSWER 7 OF 70 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998350157 MEDLINE
DOCUMENT NUMBER: 98350157
TITLE: Antiviral activities of methylated
nordihydroguaiaretic acids. 1. Synthesis,
structure identification, and inhibition of
tat-regulated HIV transactivation.
AUTHOR: Hwu J R; Tseng W N; Gnabre J; Giza P; Huang R C
CORPORATE SOURCE: Organosilicon and Synthesis Laboratory, Department of
Chemistry, National Tsing Hua University, Hsinchu,
Taiwan 30043, Republic of China, Institute of
Chemistry, Academia Sinica, Nankang, Taipei, Taiwan
11529, Republic of China, and Departmen.
CONTRACT NUMBER: 1 RO1 DE12165 (NIDR)
SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (1998 Jul 30) 41 (16)
2994-3000.
Journal code: J0F. ISSN: 0022-2623.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199810
ENTRY WEEK: 19981004
AB Nordihydroguaiaretic acid (NDGA, meso-1)
possesses four phenolic hydroxyl groups. Treatment of
NDGA with 0.50-4.1 equiv of dimethyl sulfate and 3.0-6.0
equiv of potassium carbonate in acetone at 56 degrees C gave nine
methylated products. Eight of those mono-, di-, tri-, and
tetra-O-methylated NDGAs were isolated in pure form, and
their structures were identified unambiguously by spectroscopic
methods. A preparative amount of tetramethyl NDGA M4N (10)
was obtained in 99% yield from NDGA by use of 4.1 equiv of
dimethyl sulfate for the methylation. Among the eight different
methylated NDGAs (2-6 and 8-10), tetra-O-methyl-
NDGA (10) showed the strongest anti-HIV activity (IC50 11
microM). Chemically synthesized 3'-O-methyl-NDGA ((+/-)-2)
showed identical anti-HIV activity (IC50 25 microM) to the lignan
isolated from Creosote Bush. Lignans with methylated catecholic
hydroxyl groups can be produced in large quantities with low cost.
At drug concentrations below 30 microM tetramethyl NDGA
(10) was a stronger anti-HIV agent than mono- and dimethylated
NDGAs.

Searcher : Shears 308-4994

08/882499

L37 ANSWER 8 OF 70 TOXLIT

ACCESSION NUMBER: 1998:136179 TOXLIT

DOCUMENT NUMBER: CA-129-310451Z

TITLE: Human immunodeficiency virus type 1 cDNA
integration: new aromatic hydroxylated
inhibitors and studies of the
inhibition mechanism.

AUTHOR: Farnet CM; Wang B; Hansen M; Lipford JR; Zalkow L;
Robinson WEJ; Siegel J; Bushman F

CORPORATE SOURCE: Salk Institute for Biological Studies, La Jolla

SOURCE: Antimicrob. Agents Chemother., (1998). Vol. 42, No.
9, pp. 2245-2253.

CODEN: AMACCQ. ISSN. 0066-4804.

PUB. COUNTRY: UNITED STATES

DOCUMENT TYPE: Journal; Journal Article

FILE SEGMENT: CA

LANGUAGE: English

OTHER SOURCE: CA 129:310451

ENTRY MONTH: 199812

AB Integration of the HIV-1 cDNA is a required step for viral replication. Integrase, the virus-encoded enzyme important for integration, was not yet exploited as a target for clin. useful inhibitors. Here we report on the identification of new polyhydroxylated arom. inhibitors of integrase including ellagic acid, purpurogallin, 4,8,12-trioxatricornan, and hypericin, the last of which is known to inhibit viral replication. These compds. and others were characterized in assays with subviral preintegration complexes (PICs) isolated from HIV-1-infected cells. Hypericin was found to inhibit PIC assays, while the other compds. tested were inactive.

Counterscreening of these and other integrase inhibitors against addnl. DNA-modifying enzymes revealed that none of the polyhydroxylated arom. compds. are active against enzymes that do not require metals (methylases, a pox virus topoisomerase). However, all were cross-reactive with metal-requiring enzymes (restriction enzymes, a reverse transcriptase), implicating metal atoms in the inhibitory mechanism. In mechanistic studies, we localized binding of some inhibitors to the catalytic domain of integrase by assaying competition of binding by labeled nucleotides. These findings help elucidate the mechanism of action of the polyhydroxylated arom. inhibitors and provide practical guidance for further inhibitor development.

L37 ANSWER 9 OF 70 SCISEARCH COPYRIGHT 1999 ISI (R)

ACCESSION NUMBER: 1998:298964 SCISEARCH

THE GENUINE ARTICLE: ZG375

TITLE: Inhibition of nuclear factor kappa B by
direct modification in whole cells - Mechanism of
Searcher : Shears 308-4994

action of nordihydroguaiaritic acid, curcumin and thiol modifiers

AUTHOR: Brennan P (Reprint); O'Neill L A J
 CORPORATE SOURCE: IMPERIAL CANC RES FUND, LYMPHOCYTE ACTIVAT LAB, 44 LINCOLNS INN FIELDS, LONDON WC2A 3PX, ENGLAND
 (Reprint); TRINITY COLL DUBLIN, DEPT BIOCHEM, DUBLIN, IRELAND
 COUNTRY OF AUTHOR: ENGLAND; IRELAND
 SOURCE: BIOCHEMICAL PHARMACOLOGY, (1 APR 1998) Vol. 55, No. 7, pp. 965-973.
 Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.
 ISSN: 0006-2952.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 40

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB This study was set up to investigate the mechanism of four inhibitors of interleukin-1 (IL-1)-alpha and tumor necrosis factor-(TNF)alpha activated nuclear factor kappa B (NF kappa B) in whole cells. The compounds fall into two classes: the first comprised two chain-breaking antioxidants, curcumin (diferulolylmethane) and nordihydroguaiaritic acid. The second class were two thiol-modifying agents, N-ethylmaleimide (NEM) and 2-chloro-1,3-dinitrobenzene (CDNB). Both sets of compounds were found to inhibit NF kappa B in tumour necrosis factor-activated Jurkat T lymphoma cells and interleukin 1-activated EL4.NOB-1 thymoma cells as determined by electrophoretic mobility shift assay using a specific NF kappa B DNA probe. In unstimulated cells the compounds were found to modify NF kappa B prior to chemical dissociation with sodium deoxycholate. They also inhibited DNA binding by NF kappa B when added to nuclear extracts from stimulated cells. Both of these effects occurred over a concentration range comparable to that which inhibited cytokine-activated NF kappa B in intact cells. All four agents were found to react directly with the p50 subunit of NF kappa B. However, only the antioxidants, curcumin and nordihydroguaiaritic acid (NDGA) were found to inhibit I kappa B alpha degradation activated by tumour necrosis factor-alpha. These results suggest that NF kappa B itself is susceptible to direct inhibition by a range of pharmacological agents. Furthermore, curcumin and nordihydroguaiaritic acid inhibit NF kappa B by interfering with I kappa B alpha degradation and reacting with p50 in the NF kappa B complex. These findings are likely to be useful in the attempt to develop agents which inhibit NF kappa B-dependent gene transcription. (C) 1998 Elsevier Science Inc.

L37 ANSWER 10 OF 70 MEDLINE

DUPLICATE 3

ACCESSION NUMBER: 1998158730

MEDLINE

DOCUMENT NUMBER: 98158730

TITLE: Retrograde trafficking of both Golgi complex and TGN
markers to the ER induced by
nordihydroguaiaretic acid and cyclofenil
diphenol.

AUTHOR: Drecktrah D; de Figueiredo P; Mason R M; Brown W J

CORPORATE SOURCE: Section of Biochemistry, Cornell University, Ithaca,
NY 14853, USA.

CONTRACT NUMBER: DK51596 (NIDDK)

SOURCE: JOURNAL OF CELL SCIENCE, (1998 Apr) 111 (Pt 7)
951-65.

Journal code: HNK. ISSN: 0021-9533.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199810

ENTRY WEEK: 19981002

AB Previous studies have shown that the Golgi stack and the trans-Golgi network (TGN) may play a role in capturing escaped resident endoplasmic reticulum (ER) proteins, and directing their retrograde transport back to that organelle. Whether this retrograde movement represents a highly specific or more generalized membrane trafficking pathway is unclear. To better understand both the retrograde and anterograde trafficking pathways of the secretory apparatus, we examined more closely the *in vivo* effects of two structurally unrelated compounds, the potent lipoxygenase inhibitor **nordihydroguaiaretic acid (NDGA)**

, and the non-steroidal estrogen cyclofenil diphenol (CFD), both of which are known to inhibit secretion. In the presence of these compounds, transport of vesicular stomatitis virus G membrane glycoprotein from the ER to the Golgi complex, and from the TGN to the cell surface, was inhibited potently and rapidly. Surprisingly, we found that NDGA and CFD stimulated the rapid, but not concomitant, retrograde movement of both Golgi stack and TGN membrane proteins back to the ER until both organelles were morphologically absent from cells. Both NDGA - and CFD-stimulated TGN and Golgi retrograde membrane trafficking were inhibited by microtubule depolymerizing agents and energy poisons. Removal of NDGA and CFD resulted in the complete, but not concomitant, reformation of both Golgi stacks and their closely associated TGN compartments. These studies suggest that NDGA and CFD unmask a generalized bulk recycling pathway to the ER for both Golgi and TGN membranes and, further, that NDGA and CFD are useful for investigating the molecular mechanisms that control the formation and maintenance of

Searcher : Shears 308-4994

08/882499

both the Golgi stack proper and the TGN.

L37 ANSWER 11 OF 70 JICST-EPlus COPYRIGHT 1999 JST
ACCESSION NUMBER: 980372843 JICST-EPlus
TITLE: Protective Effect of Linoleic Acid on IFN
.GAMMA.-Induced Cellular Injury in Primary Culture
Hepatocytes.
AUTHOR: LIANG J F
AKAIKE T
CORPORATE SOURCE: Tsinghua Univ., Beijing, CHN
Tokyo Inst. Technol., Yokohama
SOURCE: J Biochem, (1998) vol. 123, no. 2, pp. 213-218.
Journal Code: F0286A (Fig. 6, Tbl. 1, Ref. 38)
CODEN: JOBIAO; ISSN: 0021-924X
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New

AB We have previously demonstrated that treatment of hepatocytes with IFN .GAMMA. results a series of cellular injury processes, including DNA synthesis arrest, membrane breakage and apoptosis. In the present work, we show that IFN .GAMMA. suppresses cellular respiration and protein synthesis in hepatocytes, and that cellular respiration suppression is an early event in the IFN .GAMMA.-induced cellular injuries. Polyunsaturated fatty acids (PUFAs) increased cellular respiration of hepatocytes, but only linoleic acid showed some protective effect against IFN .GAMMA.-induced cellular respiration suppression. Linoleic acid also reduced other IFN .GAMMA.-mediated cellular injuries, including membrane breakage and protein synthesis inhibition. Like linoleic acid, fetal bovine serum also inhibited IFN .GAMMA.-induced cellular damage. Increased NAD levels were found in both IFN .GAMMA.-treated and non-treated hepatocytes following the addition of PUFAs, but clofibrate, a peroxisome proliferator, bromophenacyl bromide (BPB), an inhibitor of phospholipase, nordihydroguaiaretic acid (NDGA), an inhibitor of lipoxygenase, and arachidonic acid, a metabolite of linoleic acid, did not inhibit IFN .GAMMA.-induced cellular injury. In addition, the combination of linoleic acid and IFN .GAMMA. induced nitric oxide (NO) synthesis in hepatocytes. These results suggest that fatty acid may play an important role in liver homeostasis during chronic inflammatory states and sepsis. (author abst.)

L37 ANSWER 12 OF 70 JICST-EPlus COPYRIGHT 1999 JST
ACCESSION NUMBER: 980504553 JICST-EPlus
TITLE: Involvement of NF-.KAPPA.B activation in the induction of type II nitric oxide synthase in human
Searcher : Shears 308-4994

08/882499

glioblastoma cells.

AUTHOR: KOBAYASHI M; SUZUKI T; SUZUKI I; LIOU S-Y; HASHIMOTO Y; HASHIMOTO K
CORPORATE SOURCE: Nippon Glaxo Ltd., Ibaraki, JPN
SOURCE: Biomed Res, (1998) vol. 19, no. 2, pp. 117-126.
Journal Code: Z0236B (Fig. 7, Ref. 52)
ISSN: 0388-6107
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New

AB Nitric oxide (NO) produced by glial cells has been implicated in the pathogenesis of neurodegenerative diseases. In human glial cells, the transcriptional mechanism of inducible NO synthase (iNOS) remains to be understood. We examined the role of the transcription factor NF-.KAPPA.B in the induction of iNOS in a human glioblastoma cell line, A-172. Treatment of A-172 cells with lipopolysaccharide (LPS), interleukin-1.BETA.(IL-1.BETA.) and interferon-.GAMMA. (IFN-.GAMMA.) induced iNOS mRNA and protein expression subsequent to the degradation of I.KAPPA.B, a protein that inhibits NF-.KAPPA.B, and the DNA binding of NF-.KAPPA.B. Furthermore, the antioxidant pyrroridine dithiocarbamate (PDTC), which is known to inhibit NF-.KAPPA.B activation, inhibited nitrite production in a dose-dependent manner. The inhibitory effect of PDTC correlated with the prevention of I.KAPPA.B degradation. Another antioxidant, nordihydroguaiaretic acid (NDGA), also inhibited the nitrite formation and iNOS mRNA expression through its preventive effect on NF-.KAPPA.B activation. These results suggest the involvement of NF-.KAPPA.B activation in iNOS induction in human glial cells.
(author abst.)

L37 ANSWER 13 OF 70 TOXLINE

ACCESSION NUMBER: 1997:119509 TOXLINE
DOCUMENT NUMBER: BIOSIS-97-20930
TITLE: Clostridium difficile toxin A induces the release of neutrophil chemotactic factors from rat peritoneal macrophages: Role of interleukin-1beta, tumor necrosis factor alpha, and leukotrienes.
AUTHOR: ROCHA M F G; MAIA M E T; BEZERRA L R P S; LYERLY D M; GUERRANT R L; RIBEIRO R A; LIMA A A M
CORPORATE SOURCE: Clinical Res. Unit, Federal Univ. Ceara, PO Box 3229, CEP 60 436-160, Fortaleza, CE, Brazil.
SOURCE: INFECTION AND IMMUNITY, (1997). Vol. 65, No. 7, pp. 2740-2746.
CODEN: INFIBR.
FILE SEGMENT: BIOSIS
LANGUAGE: English

Searcher : Shears 308-4994

08/882499

ENTRY MONTH: 199709

AB BIOSIS COPYRIGHT: BIOL ABS. Clostridium difficile produces a potent enterotoxin and cytotoxin, toxins A and B, respectively, which appear to be responsible for pseudomembranous colitis and antibiotic-associated diarrhea. In the present study we explored the neutrophil migration evoked by toxin A in the peritoneal cavities and subcutaneous air pouches of rats and examined the role of macrophages and their inflammatory mediators in this process. Toxin A causes a significant dose-dependent neutrophil influx into the peritoneal cavity, with a maximal response at 0.1 mug/ml and at 4 h. The depletion of macrophages by peritoneal washing prevents the toxin A-induced neutrophil migration into the peritoneal cavity. In contrast, an increase in macrophages induced by peritoneal injection of thioglycolate amplifies this toxin effect on neutrophil migration. Furthermore, the injection of supernatants from toxin A-stimulated macrophages into the rat peritoneal cavity causes significant neutrophil migration. Pretreatment of rats with BWA4C, nordihydroguaiaretic acid, mepacrine, or dexamethasone inhibits the neutrophil migration evoked by toxin A in the peritoneal cavities. However, pretreatment with the cyclooxygenase inhibitor indomethacin or the platelet-activating factor antagonist BN52021 fails to alter toxin A-induced neutrophil migration. Toxin A was also injected into air pouches of normal rats or rats pretreated with anti-interleukin-1beta (anti-IL-1beta) or anti-tumor necrosis factor alpha (anti-TNF-alpha) antibodies. Anti-TNF-alpha or anti-IL-1beta antibodies significantly reduce the neutrophil migration induced by toxin A. These data suggest that neutrophil migration evoked by toxin A is in part dependent on macrophage-derived cytokines, such as TNF-alpha and IL-1beta, and leukotrienes. These mediators may help to explain the intense inflammatory colitis caused by C. difficile toxin A in an experimental animal model of this disease.

L37 ANSWER 14 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97242020 EMBASE

DOCUMENT NUMBER: 1997242020

TITLE: Dermatologic drugs, pregnancy, and lactation: A conservative guide.

AUTHOR: Reed B.R.

CORPORATE SOURCE: Dr. B.R. Reed, 2200 E 18th Ave, Denver, CO 80206,
United States

SOURCE: Archives of Dermatology, (1997) 133/7 (894-898).

Refs: 38

ISSN: 0003-987X CODEN: ARDEAC

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 010 Obstetrics and Gynecology

013 Dermatology and Venereology

037 Drug Literature Index

Searcher : Shears 308-4994

08/882499

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB No database for determination of precise risk of drug use during pregnancy and lactation is available. There are, however, educated opinions concerning the advisability of use of a drug during the childbearing years from manufacturers, the Food and Drug Administration, various teratologists, the American Academy of Pediatrics, and the World Health Organization. Not all medications are absolutely contraindicated during pregnancy and lactation. Some drugs have been extensively used without apparent adverse effects in the mother or infant. When it is necessary to select a medication for use during pregnancy or lactation, the medication should have minimal risk. This article summarizes dermatologic drugs whose known risk is low.

L37 ANSWER 15 OF 70 MEDLINE

DUPLICATE 4

ACCESSION NUMBER: 97184665 MEDLINE

DOCUMENT NUMBER: 97184665

TITLE: Activation of the NF-kappaB transcription factor in a T-lymphocytic cell line by hypochlorous acid.

AUTHOR: Schoonbroodt S; Legrand-Poels S; Best-Belpomme M; Piette J

CORPORATE SOURCE: Laboratory of Virology, Institute of Pathology B23, University of Liege, Belgium.

SOURCE: BIOCHEMICAL JOURNAL, (1997 Feb 1) 321 (Pt 3) 777-85.
Journal code: 9Y0. ISSN: 0264-6021.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199705

ENTRY WEEK: 19970503

AB Reactive oxygen species (ROS) such as hydrogen peroxide serve as second messengers in the induction of the transcription factor NF-kappaB, and hence in the activation and replication of human immunodeficiency virus type 1 (HIV-1) in human cells.

During inflammatory reactions, many oxidative species are produced, one of which is hypochlorous acid (HOCl), which is responsible for the microbicidal effects of activated human polymorphonuclear leukocytes. Treatment of a T-lymphocytic cell line with micromolar concentrations of HOCl promoted the appearance of transcription factor NF-kappaB (the heterodimer p50/p65) in the nucleus of the cells, even in the absence of de novo protein synthesis. Western blot analysis of the NF-kappaB inhibitory subunits (IkappaB) demonstrated that both IkappaB-alpha proteolysis and p105 processing were induced by the treatment.

NF-kappaB activation was very effective when cells were subjected to hyperthermia before being treated with HOCl. Various

Searcher : Shears 308-4994

antioxidants, such as pyrrolidine dithiocarbamate, p-bromophenacyl-bromide and **nordihydroguaiaretic acid** could strongly reduce NF-kappaB translocation, demonstrating the importance of oxidative species in the transduction mechanism. Moreover, ACH-2 cells treated with HOCl or H₂O₂ released tumour necrosis factor-alpha (TNF-alpha) in the supernatants. The importance of TNF-alpha release in NF-kappaB induction by HOCl or H₂O₂ was demonstrated by the fact that: (1) the nuclear appearance of NF-kappaB was promoted in untreated cells; and (2) synergism between TNF-alpha and HOCl was detected. Collectively, these results suggest that HOCl should be considered as an oxidative species capable of inducing NF-kappaB in a T-lymphocytic cell line through a transduction mechanism involving ROS, and having a long-distance effect through subsequent TNF-alpha release.

L37 ANSWER 16 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD

ACCESSION NUMBER: 97-19242 DRUGU P

TITLE: Biological activity of magnolol: a review.

AUTHOR: Sarker S D

CORPORATE SOURCE: Univ.Exeter

LOCATION: Exeter, U.K.

SOURCE: Fitoterapia (68, No. 1, 3-8, 1997) 1 Fig. 1 Tab. 43

Ref.

CODEN: FTRPAE ISSN: 0367-326X

AVAIL. OF DOC.: Department of Biological Sciences, University of Essex,
Washington Singer Laboratories, Perry Road, Exeter,
Devon, EX4 4QG, England.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 97-19242 DRUGU P

AB The biological activity of magnolol (MG) is reviewed. MG is a CNS depressant and muscle relaxant, and has antiplatelet, antitumor, insecticidal, antioxidant and antimicrobial actions. MG

inhibits sperm motility and carrageenan- (CG) and arachidonic acid- (AA) induced 5-HT release from platelets, and inhibits tetradecanylphorbolacetate- (TPA) induced papilloma formation. MG inhibits CG-induced paw edema and acetic acid- (AC) induced writhing. MG reduces A23187-induced pleurisy and copper sulfate pentahydrate- (CSP) induced emesis. Indomethacin (IN), honokiol (HK), dexamethasone (DM), monoterpenylmagnolol (MM), Saiboku-To (ST), glycyrrhizin (GL), metergoline (MT), tocopherol (TC), **nordihydroguaiaretic acid** (NA), propranolol (PP), cyproheptadine (CH) and tetrodotoxin (TTX) are all mentioned.

ABEX MG is a potent CNS depressant and has muscle relaxant activity. MG has antimicrobial and antiplatelet activity and is a Ca²⁺ blocker. MG, HK and MM inhibit Epstein-Barr virus early

Searcher : Shears 308-4994

antigen activation on Raji cells induced by TPA. MG inhibits mouse skin tumor promotion in an in-vivo 2-stage carcinogenesis test. MG applied before TPA delayed papilloma formation in mouse skin. While tail bleeding time of mice is prolonged by MG, it does not prevent acute thromboembolic death in mice. MG inhibits CG-and AA-induced 5-HT release from platelet suspension. MG inhibits CG-induced mouse hind-paw edema and AC-induced writhing. MG reduces the lethality of endotoxin challenge and recovers myeloperoxidase activity in edematous paw but is less effective than IN. Unlike DM, MG does not increase liver glycogen levels. MG reduces A23187-induced protein leakage and PMN infiltration in a mouse pleurisy model. MG appears to be responsible for the antiasthmatic effects of ST. MG is less potent than GL as an inhibitor of 11beta-hydroxysteroid dehydrogenase. In isolated rat heart mitochondria, MG and HK are more potent antioxidants than TC. MG inhibits UV-induced mutagenesis, and inhibits the emetic action of CSP in frogs. MG and HK are more effective than NA in inhibiting the acetyltransferase activity in rat spleen microsomes and membrane fractions of human PMN. MG and HK inhibit A23187-induced PAF production in human PMN. MG inhibits K+-stimulated 5-HT release from rat cortex, effects unchanged by MT, PP, CH or TTX. MG inhibits lipid peroxidation in sperm. (RPG)

L37 ANSWER 17 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1996-209296 [21] WPIDS
 DOC. NO. CPI: C96-066743
 TITLE: New 1,4-Bis-(3,4-di hydroxyphenyl)-2,3-di methyl-butane derivs. - are isolated from extracts of creosote bush, useful for suppressing Tat transactivation of a lentivirus, including HIV.
 DERWENT CLASS: B05
 INVENTOR(S): GNABRE, J N; HUANG, R; HUANG, R C C; HUANG, R C
 PATENT ASSIGNEE(S): (UYJO) UNIV JOHNS HOPKINS
 COUNTRY COUNT: 22
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9610549	A1	960411	(9621)*	EN	61
RW:	AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE				
W:	AU CA CN JP				
AU 9536339	A	960426	(9631)		
EP 783474	A1	970716	(9733)	EN	
R:	AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE				
US 5663209	A	970902	(9741)	17	
Searcher : Shears 308-4994					

08/882499

JP 10509421 W 980914 (9847) 45
AU 700481 B 990107 (9913)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9610549	A1	WO 95-US11779	950922
AU 9536339	A	AU 95-36339	950922
EP 783474	A1	EP 95-933830	950922
		WO 95-US11779	950922
US 5663209	A Div ex	US 94-316341	940930
		US 96-627588	960404
JP 10509421	W	WO 95-US11779	950922
		JP 96-511844	950922
AU 700481	B	AU 95-36339	950922

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9536339	A Based on	WO 9610549
EP 783474	A1 Based on	WO 9610549
JP 10509421	W Based on	WO 9610549
AU 700481	B Previous Publ.	AU 9536339
	Based on	WO 9610549

PRIORITY APPLN. INFO: US 94-316341 940930; US 96-627588 960404

AN 1996-209296 [21] WPIDS

AB WO 9610549 A UPAB: 19970516

1,4-Bis-(3,4-dihydroxyphenyl)-2,3-

dimethyl-butane derivs. of formula (I) are new:

R1-R4 = OH, OMe or OC(O)Me, provided that not all are OH. Also claimed is a method for suppressing Tat transactivation of a lentivirus comprising the admin. to a cell of extracts of Larrea tridentata having the gas chromatography profiles shown in the specification.

USE - (I) and 1,4-bis-(3,4-dihydroxyphenyl)-2,3-dimethylbutane are useful for suppressing Tat transactivation of a lentivirus (claimed), including the HIV virus.

ADVANTAGE - Extract of Larrea tridentata also inhibits HIV cytopathic effects on human lymphoblastoid cells chronically infected with the virus.

Dwg.0/7

ABEQ US 5663209 A UPAB: 19971013

A method for the suppression of Tat transactivation of a lentivirus in a cell comprising the steps of: (a) administering to the cell an effective amount of a compound of formula (I); and (b) allowing the compound to suppress Tat transactivation of the lentivirus in the

Searcher : Shears 308-4994

08/882499

cell.
Dwg. 0/7

L37 ANSWER 18 OF 70 TOXLIT

ACCESSION NUMBER: 1996:118626 TOXLIT
DOCUMENT NUMBER: CA-125-076343J
TITLE: Nordihydroguaiaretic acid derivatives for
the suppression of HIV Tat transactivation.
AUTHOR: Huang RC; Gnabbe JN
SOURCE: (1996). PCT Int. Appl. PATENT NO. 96 10549 04/11/96
(Johns-Hopkins University).
PUB. COUNTRY: United States
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 125:76343
ENTRY MONTH: 199609

AB The invention reveals the isolation, purifn. and characterization from the creosote bush Larrea tridentata of compds. I [R1-R4 = OH, OMe, CH₃C(O)O, provided that R1-R4 are not each OH simultaneously]. Each compd. is a deriv. of 1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane (nordihydroguaiaretic acid, NDGA). In addn., NDGA and each deriv. can be used in a method to suppress Tat transactivation of a lentivirus, including the HIV virus, in a cell by administering NDGA or a deriv. of NDGA to the cell. Fractionation of NDGA derivs. from Larrea tridentata is described. Inhibition of transactivation of HIV promoter activity by NDGA and 4-O-methyl-NDGA was detd.

L37 ANSWER 19 OF 70 MEDLINE

DUPPLICATE 5

ACCESSION NUMBER: 96389991 MEDLINE
DOCUMENT NUMBER: 96389991
TITLE: Inhibition of vesicle-mediated protein transport by nordihydroguaiaretic acid.
AUTHOR: Tagaya M; Henomatsu N; Yoshimori T; Yamamoto A;
Tashiro Y; Mizushima S
CORPORATE SOURCE: School of Life Science, Tokyo University of Pharmacy
and Life Science.
SOURCE: JOURNAL OF BIOCHEMISTRY, (1996 May) 119 (5) 863-9.
Journal code: HIF. ISSN: 0021-924X.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
AB Nordihydroguaiaretic acid (NDGA) blocks
intra-Golgi protein transport in a cell-free system and prolactin
Searcher : Shears 308-4994

secretion from GH3 cells [Tagaya, M., Henomatsu, N., Yoshimori, T., Yamamoto, A., Tashiro, Y., and Fukui, T. (1993) FEBS Lett. 324, 201-204]. To determine which intracellular secretory pathway(s) is inhibited by NDGA, we investigated its effect on the transport of the vesicular stomatitis virus-encoded glycoprotein in BHK-21 cells. NDGA blocked protein transport from the endoplasmic reticulum to the Golgi apparatus, and from the trans-Golgi network to the plasma membrane. In addition, it retarded the brefeldin A-induced retrograde transport of mannosidase II to the endoplasmic reticulum. Although NDGA had an inhibitory effect on protein synthesis, it induced the expression of BiP, a chaperone located in the endoplasmic reticulum. The induction of BiP may be a consequence of the inhibition of protein transport by NDGA.

L37 ANSWER 20 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD

ACCESSION NUMBER: 96-04638 DRUGU M A

TITLE: Isolation of anti-HIV-1 lignans from *Larrea tridentata* by counter-current chromatography.

AUTHOR: Gnabre J N; Ito Y; Ma Y; Huang R C

CORPORATE SOURCE: Univ.Johns-Hopkins; Nat.Inst.Health-Bethesda

LOCATION: Baltimore; Bethesda, Md., USA

SOURCE: ; J.Chromatogr. (719, No. 2, 353-64, 1996) 10 Fig. 1

Tab. 26 Ref.

CODEN: ; JOCR

AVAIL. OF DOC.: Department of Biology, The Johns Hopkins University, 144 Mudd Hall, 3400 N. Charles Street, Baltimore, MD 21218-2685, U.S.A. (R.C.H.).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 96-04638 DRUGU M A

AB The results of this paper indicate that the desert creosote bush, *Larrea tridentata*, is a source for new lignans with anti-HIV activity. These compounds inhibited Tat-induced transactivation, being the first plant-derived agents to do so. A powerful bioassay, involving constructs of HIV LTR promotor and reporter gene, the secreted alkaline phosphatase (Seap) and CMV promotor-driven Tat, was established for screening potential HIV inhibitors. Counter-current chromatography (CCC) was used to isolate several lignans from the active fractions of *L. tridentata*. One of the compounds, mal.4, was found to be a strong inhibitor of HIV transcription, HIV Tat-regulated transactivation and HIV replication.

ABEX Using the Seap bioassay of HIV Tat transactivation and the 2-phase hexane-ethyl acetate-methanol-water solvent system, 2 major components (Gr and Lo) were identified as anti-HIV active principles. The chemical structures of the constituents of Gr

Searcher : Shears 308-4994

08/882499

(G1-G4) and Lo (L1-L4) were determined by GC-MS and NMR. After optimization of the isolation conditions, a large-scale isolation with the chloroform-methanol-water system yielded 5 constituents (FB1-FB5). The most predominant anti-HIV compound FB2, denoted Malachi 4:5-6 or mal.4 (heminordihydroguaiaretate), which occurs in 0.23% yield, was separated from its FB1 isomer (0.13% yield). Compound FB4 and the 2 tricyclic lignans (FB3 and FB5) were also isolated in a substantial amount for further testing of their anti-HIV activities. A total of 16 lignans of *L. tridentata* were identified in this study. Eight of these were structurally new. Although previously described, the lignan 3'-O-methyl NDGA (mal.4) is now known for its anti-HIV activity. Mal.4 exerted its inhibitory activity by interfering with the binding of Sp1 protein to HIV LTR, thus blocking the proviral transcription, Tat transactivation, and suppressing viral replication. (LP)

L37 ANSWER 21 OF 70 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 96310313 MEDLINE

DOCUMENT NUMBER: 96310313

TITLE: Effects of cellular aging on the induction of c-fos by antioxidant treatments.

AUTHOR: Keogh B P; Tresini M; Cristofalo V J; Allen R G

CORPORATE SOURCE: Center for Gerontological Research, Medical College of Pennsylvania, Philadelphia 19129, USA.

CONTRACT NUMBER: AG00378 (NIA)
AG00131 (NIA)
AG00523 (NIA)

+
CONTRACT NUMBER: AG00378 (NIA)
AG00131 (NIA)
AG00523 (NIA)

SOURCE: MECHANISMS OF AGEING AND DEVELOPMENT, (1996 Mar 29)
86 (3) 151-60.
Journal code: LMJ. ISSN: 0047-6374.

PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199701

ENTRY WEEK: 19970104

AB The proto-oncogene c-fos (the cellular homolog of v-fos, Finkel-Biskis-Jenkins (FBJ) murine osteogenic sarcoma virus) encodes a major component of the activator protein-1 (AP-1) transcription factor. Serum stimulation as well as oxidizing treatments induce transitory increases in c-fos mRNA abundance. The induction of c-fos by serum stimulation is also known to decline during proliferative senescence. In this study, we examined the effects of two classes of antioxidants on the induction of c-fos in early and late passage human fetal lung fibroblasts (WI-38). N-acetyl cysteine (NAC) induces c-fos transcription in both early and late passage cells, while nordihydroguaiaretic

Searcher : Shears 308-4994

acid (NGA) induced c-fos transcription in early passage cells but fails to stimulate it in late passage cells. Since we had previously observed an age-related decline in protein kinase C (PKC) translocation from the cytosol to the membrane, following its activation, and because PKC activation appears to be involved in the NGA induction of c-fos we examined the relative protein abundances of several PKC isoforms in early and late passage cells.

Additionally, we examined the protein abundance of several members of the MAP kinase pathway which could play a role in c-fos induction by the PKC-dependent pathway. We were unable to detect PKC-beta or theta in early or late passage cells. Late passage cells contained a slightly greater abundance of PKC alpha, gamma and epsilon than cells at an early passage. No other differences in PKC isoforms or in members of the MAP kinase family were observed in early or late passage cells. These results clearly demonstrate that at least some pathways leading to c-fos induction remain intact in late passage cells. While we were unable to detect any decreases in PKC isoforms or MAP kinase proteins we cannot exclude the possibility that functional decrements accumulate in these proteins during senescence.

L37 ANSWER 22 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96059956 EMBASE

DOCUMENT NUMBER: 1996059956

TITLE: Alterations in reactive oxygen, pH, and calcium in astrocytoma cells during lethal injury.

AUTHOR: Wu Y.; Taylor B.M.; Sun F.F.

CORPORATE SOURCE: Cell Biology/Inflammation Res. Dept., Upjohn Laboratories, Kalamazoo, MI 49001, United States

SOURCE: American Journal of Physiology - Cell Physiology, (1996) 270/1 39-1 (C115-C124).

ISSN: 0363-6143 CODEN: AJPCDD

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 002 Physiology
005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Exposure of cultured human astrocytoma cells to iodoacetic acid results in rapid depletion of cellular ATP and cell death. Pathophysiological changes in the injured cells, including formation of reactive oxygen species (ROS), cell viability, glutathione, pH, and cytosolic calcium, were characterized at the cellular level via fluorescence microscopy. After iodoacetic acid treatment, cellular ATP and intracellular glutathione fell sharply to undetectable levels within 2 h. ROS, as detected by the oxidation of dichlorofluorescein, appeared in 20 min and reached a maximum before the loss of membrane integrity. Cells became acidotic within 10 min.

Searcher : Shears 308-4994

Cytosolic free calcium concentration exhibited a slow increase and then a sharp influx shortly before the rupture of the cell membrane. The addition of lipophilic antioxidants, nordihydroguaiaretic acid or the troloxamine U-78517F, eliminated the accumulation of ROS and delayed the onset of cell death without affecting other parameters observed in the early phase of the injury. We conclude that ROS is formed and may play important roles during lethal cell injury caused by energy depletion.

L37 ANSWER 23 OF 70 TOXLIT

ACCESSION NUMBER: 1996:63015 TOXLIT
 DOCUMENT NUMBER: CA-124-167496G
 TITLE: Enhancement of introduction of foreign matter into higher eukaryotic cells by co-introduction of anti-apoptosis or anti-inflammatory substances.
 AUTHOR: Cotten M; Baker A; Chiocca S
 SOURCE: (1995). PCT Int. Appl. PATENT NO. 95 33062 12/07/95 (Boehringer Ingelheim International GmbH).
 PUB. COUNTRY: Germany: Germany, Federal Republic of
 DOCUMENT TYPE: Patent
 FILE SEGMENT: CA
 LANGUAGE: German
 OTHER SOURCE: CA 124:167496
 ENTRY MONTH: 199605

AB The toxicity problems arising when foreign matter is introduced into higher eukaryotic cells, esp. with transfection with DNA, are obviated by expression in the cell of gene products that block the apoptosis induced by the transfection process and/or by treating the cells with anti-inflammatory substances. Preferred anti-apoptosis genes are Bcl-2, adenovirus E1B 19K or an anti-apoptotic gene of the CELO avian adenovirus. The preferred anti-inflammatory substance is adenovirus VA1, which is introduced into the cell in the form of VA1 DNA. These measures help to achieve a long-lasting gene expression. The anti-apoptotic gene of CELO virus was cloned and sequenced. The enhancement by the above genes of mammalian cell transfection using transferrin (or streptavidin)-polylysine conjugate/adenovirus transfection complexes was demonstrated. The synergistic effect of anti-inflammatory compds. such as glucocorticoids, ibuprofen, etc. was also shown.

L37 ANSWER 24 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 95326741 EMBASE
 DOCUMENT NUMBER: 1995326741
 TITLE: Characterization of anti-HIV lignans from *Larrea tridentata*.
 AUTHOR: Gnabre J.; Huang R.C.C.; Bates R.B.; Burns J.J.; Calderea S.; Malcomson M.E.; McClure K.J.
 CORPORATE SOURCE: Department of Biology, Johns Hopkins University, Baltimore, MD 21218-2685, United States
 Searcher : Shears 308-4994

08/882499

SOURCE: Tetrahedron, (1995) 51/45 (12203-12210).
ISSN: 0040-4020 CODEN: TETRAB
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index

LANGUAGE :

SUMMARY LANGUAGE: English

AB Fractions from *Larrea tridentata* with anti-HIV-1 activity (specifically, inhibition of HIV Tat transactivation) were analyzed by GC/MS and found to contain lignans 1a-i and 2a-d. Assay-guided purification by countercurrent chromatography established 1g (mal. 4) to be especially active. Compounds 1b-f, h, i and 2d are new.

L37 ANSWER 25 OF 70 MEDLINE

DUPPLICATE 7

ACCESSION NUMBER: 96074683 MEDLINE

DOCUMENT NUMBER: 96074683

TITLE: Inhibition of human immunodeficiency virus type 1 transcription and replication by RNA sequence-selective plant lignans

AUTHOR: Gnabre J N; Brady J N; Clanton D J; Ito Y; Dittmer J;
Fates R B; Huang P C

CORPORATE SOURCE: Bates R B, Huang K C
Department of Biology, Johns Hopkins University,
Baltimore MD 21218 USA

CONTRACT NUMBER:

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF
THE UNITED STATES OF AMERICA, (1995 Nov 21) 92 (24)
11239-43.

Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199602

AB A plant lignan, 3'-O-methyl nordihydroguaiaretic

(3'-O-methyl NDGA, de-

molecular weight 316), was isolated from *Larrea tridentata* and found to be able to inhibit human immunodeficiency virus (HIV) Tat-regulated transactivation in vivo, induce protection of lymphoblastoid CEM-SS cells from HIV (strain IIIB) killing, and suppress the replication of five HIV-1 strains (WM, MN, VS, JR-CSF, and IIIB) in mitogen-stimulated peripheral blood mononuclear cells, all in a dose-dependent manner. Mal.4 inhibits both basal transcription and Tat-regulated transactivation in vitro. The target of Mal.4 has been localized to nucleotides -87 to -40 of the HIV long terminal repeat. Mal.4 directly and specifically interferes with the binding of Sp1 to Sp1 sites in the HIV long terminal

Searcher : Shears 308-4994

repeat. By inhibiting proviral expression, Mal.4 may be able to interrupt the life cycles of both wild-type and reverse transcriptase or protease mutant viruses in HIV-infected patients.

L37 ANSWER 26 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS

ACCESSION NUMBER: 1996:67310 BIOSIS

DOCUMENT NUMBER: PREV199698639445

TITLE: Interactions between phytoestrogens and human sex steroid binding protein.

AUTHOR(S): Martin, Marie Elise; Haourigui, Malika; Pelissero, Catherine; Benassayag, Claudine (1); Nunez, Emmanuel A.

CORPORATE SOURCE: (1) U224 INSERM, Fac. Med. Xavier Bichat, 75870 BP 146, Paris France

SOURCE: Life Sciences, (1995) Vol. 58, No. 5, pp. 429-436.
ISSN: 0024-3205.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The interactions of human Sex steroid binding protein (SBP), and the lignans (**Nordihydroguaiaretic acid (NDGA)**) enterolactone (Ent), enterodiol (End)) and isoflavonoid phytoestrogens (Equol (Eq), diazein (Dad), genistein (Gen)) were studied. The phytoestrogens had different dose-dependent inhibitory effects on steroid binding by SBP. Their relative efficiencies were : Ent ltoreq NDGA = Eq gt Gen for displacing E2 and Eq gt Ent gt NDGA gt Gen for displacing T. End and Dad were much less active. Scatchard analysis suggested that NDGA had similar non-competitive effects on T and E2 binding by reducing the number of binding sites without changing the association constants. But Eq seemed to inhibit E2 binding noncompetitively and T binding competitively. NDGA binding to SBP reduced the immunorecognition of SBP by monospecific antiSBP antibodies, suggesting that NDGA changed SBP immunoreactivity. Unlike NDGA, Eq binding to SBP caused no immunological changes in SBP, indicating qualitative differences in the effects of the lignan and isoflavonoid. Our results indicate that phytoestrogens may modulate the SBP activity and so influence the role of this protein in the delivery of hormonal information to sex steroid-dependent cells.

L37 ANSWER 27 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE

8

ACCESSION NUMBER: 95036795 EMBASE

DOCUMENT NUMBER: 1995036795

TITLE: E1A3Y1 cell-specific toxicity of tea polyphenols and their killing mechanism.

AUTHOR: Mitsui T.; Yamada K.; Yamashita K.; Matsuo N.; Okuda A.; Kimura G.; Sugano M.

Searcher : Shears 308-4994

CORPORATE SOURCE: Laboratory Food Science/Technology, Faculty of Agriculture, Kyushu University, 6-10-1 Hakozaki, Higashi-ku, Fukuoka 812, Japan

SOURCE: International Journal of Oncology, (1995) 6/2 (377-383).

ISSN: 1019-6439 CODEN: IJONES

COUNTRY: Greece

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB To screen carcinostatic components in foodstuffs, the toxicity of tea polyphenols was compared between rat 3Y1 diploid fibroblasts and a variety of their virally transformed cells. Among tea polyphenols tested, epigallocatechin gallate killed 3Y1 cells transformed by E1A gene of human adenovirus type 12; (E1A-3Y1 cells) at a 100 times lower concentration than the parental 3Y1 cells. Epigallocatechin gallate also exerted a strong E1A-3Y1 cell-specific toxicity, while epicatechin and epicatechin gallate did not. When the activity of three antioxidant enzymes was compared between 3Y1 and its transformants, catalase activity was markedly low in the latter, especially in E1A-3Y1 cells, and the substrate of the enzyme, hydrogen peroxide, exerted a toxicity specific to this cell line. Then the inhibitory activities of various chemicals on E1A-3Y1 cell-specific toxicity of phospholipids or catechol were examined. Among lipoxygenase inhibitors, all of the polyphenolic compounds inhibited the toxicity of phospholipids, but not a nonpolyphenolic inhibitor (clofibrate). Two phospholipase A2 inhibitors (dexamethasone and quinacrine) did not inhibit the toxicity. These results indicate that the triphenol structure of the B ring is essential for the E1A-3Y1 cell-specific toxicity of tea polyphenols, and that the decrease in catalase activity is partially responsible for the higher sensitivity of E1A-3Y1 cells against the polyphenols. The inhibitory effect of polyphenolic lipoxygenase inhibitors is ascribed at least in part to their antioxidant activities.

L37 ANSWER 28 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE

9

ACCESSION NUMBER: 95063785 EMBASE

DOCUMENT NUMBER: 1995063785

TITLE: The non-steroidal anti-inflammatory drug, indomethacin, as an inhibitor of HIV replication.

AUTHOR: Bourinbaiar A.S.; Lee-Huang S.

Searcher : Shears 308-4994

08/882499

CORPORATE SOURCE: Department of Biochemistry, New York University Medical Center, 550 First Avenue, New York, NY 10016, United States
SOURCE: FEBS Letters, (1995) 360/1 (85-88).
ISSN: 0014-5793 CODEN: FEBLAL
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Indomethacin, a common non-steroidal anti-inflammatory drug (NSAID), has been used to treat rheumatoid arthritis. Although indomethacin has also been used as an immunopotentiator and symptomatic NSAID) in AIDS, its effect on HIV replication is unknown. MT-4 lymphocytes were inoculated with HIV in the presence of indomethacin and tested for p24 expression by ELISA. The 50% inhibition (IC50,) was 10 .mu.M, corresponding to plasma levels after administration of 50 mg oral indomethacin. The antiviral effect appears to be specific since no toxicity has been observed at the IC50, dose, and unrelated NSAIDs have not shown the activity at clinical doses. Indomethacin may, thus, represent a new class of anti-HIV drug.

L37 ANSWER 29 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1994-200294 [24] WPIDS
DOC. NO. CPI: C94-091594
TITLE: Identifying cpds. with neuro protective activity - against organisms causing e.g. encephalitis by inhibiting release of platelet activation factor and arachidonate metabolites.
DERWENT CLASS: B04 D16
INVENTOR(S): BERNTON, E W; GENDELMAN, H; JETT, M
PATENT ASSIGNEE(S): (USSA) US DEPT OF ARMY
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9412667	A1	940609 (9424)*	EN	40	
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: CA JP US					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9412667	A1	WO 93-US11542	931129
Searcher : Shears 308-4994			

PRIORITY APPLN. INFO: US 92-982656 921127; US 93-61970 930902

AN 1994-200294 [24] WPIDS

AB WO 9412667 A UPAB: 19940803

Screening cpds. screened for neuroprotective activity comprises (1) infecting cultured monocytes or leucocytes with an organism known to cause neuronal damage; (2) adding astrocytes and then test cpds. to the infected cultures; (3) incubating to allow prodn. of TNF (tumour necrosis factor) alpha; (4) withdrawing aliquots of supernatant and adding to neuron-contg. cultures; (5) incubating then examining cells for neurotoxic or neurocytopathic effects.

Also claimed are (1) supernatant in a culture of neurons, of a culture contg. infected monocytes/lymphocytes and astrocytes; (2) compsns. contg. neuroprotective amts. of 11-nor-delta⁸-tetrahydrocannabinol-9-carboxylic acid (I) or (for delivery through the mucosa) NDGA (nordihydroguaiaretic acid).

USE - The method detects cpds. which inhibit release of, or antagonise, arachidonate metabolites and platelet activation factor (PAF) which cause neuronal damage (encephalopathy and encephalitis) following viral (esp. HIV), parasitic or bacterial infection of the CNS. The cpds. may also include replication and release of infectious virus and, for HIV treatment, can be combined with other drugs for control of retroviral infections.

Dwg.0/0

L37 ANSWER 30 OF 70 SCISEARCH COPYRIGHT 1999 ISI (R)

ACCESSION NUMBER: 94:152416 SCISEARCH

THE GENUINE ARTICLE: NB409

TITLE:

PREFERENTIAL INHIBITION OF
PLATELET-DERIVED GROWTH FACTOR-STIMULATED
DNA-SYNTHESIS AND PROTEIN-TYROSINE PHOSPHORYLATION
BY NORDIHYDROGUAIARETIC ACID

AUTHOR: DOMIN J; HIGGINS T; ROZENGURT E (Reprint)

CORPORATE SOURCE: IMPERIAL CANC RES FUND, 44 LINCOLNS FIELDS, LONDON
WC2A 3PX, ENGLAND (Reprint); IMPERIAL CANC RES FUND,
LONDON WC2A 3PX, ENGLAND

COUNTRY OF AUTHOR: ENGLAND

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (18 MAR 1994) Vol.
269, No. 11, pp. 8260-8267.

ISSN: 0021-9258.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 56

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Nordihydroguaiaretic acid (NDGA), a reportedly specific lipoxygenase inhibitor, was found to

Searcher : Shears 308-4994

selectively inhibit platelet-derived growth factor (PDGF)-stimulated DNA synthesis in Swiss 3T3 cells. Maximal inhibition of PDGF-induced [³H]thymidine incorporation (96%) was observed using 4 μM NDGA (IC₅₀ = 1.5 μM). No effect of NDGA was observed upon DNA synthesis stimulated with either fetal bovine serum, bombesin, or epidermal growth factor (EGF) in the presence of insulin, or with the potent mitogen Pasteurella multocida toxin. The selective inhibition of PDGF-stimulated DNA synthesis by NDGA was also observed in diploid murine cells, rat, and human fibroblasts. Furthermore, 4 μM NDGA also inhibited PDGF-stimulated anchorage-independent colony growth of rat-1 cells by 76%. Using Swiss 3T3 cells, we found that PDGF-stimulated arachidonic acid mobilization and prostaglandin E(2) production was abolished by NDGA in a dose-dependent manner. Inhibition of PDGF-stimulated arachidonic acid mobilization by NDGA could not, however, explain its potent inhibitory effect upon PDGF-stimulated DNA synthesis.

Our results showed that NDGA also selectively inhibited PDGF receptor tyrosine phosphorylation in a dose-dependent manner in intact cells. Protein tyrosine phosphorylation stimulated by EGF or bombesin was not altered by NDGA treatment. Crucially, NDGA inhibited *in vitro* the tyrosine kinase activity of anti-phosphotyrosine and anti-PDGF receptor immunoprecipitates prepared from cultures stimulated with PDGF. This inhibition of receptor tyrosine phosphorylation in a cell-free system confirmed that NDGA acts directly at the level of the PDGF receptor tyrosine kinase domain. These results suggest that the potent and selective inhibitory effect of NDGA on PDGF-stimulated DNA synthesis results from its inhibitory action on tyrosine phosphorylation.

L37 ANSWER 31 OF 70 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 94333933 MEDLINE
DOCUMENT NUMBER: 94333933
TITLE: The immortalized astroglial cell line RC7 is a new model system for the study of nerve growth factor (NGF) regulation: stimulation by interleukin-1 beta and transforming growth factor-beta 1 is additive and affected differently by dibutyryl cyclic AMP.
AUTHOR: Hahn M; Lorez H; Fischer G
CORPORATE SOURCE: Pharma Division, F. Hoffmann-La Roche Ltd., Basel, Switzerland.
SOURCE: GLIA, (1994 Apr) 10 (4) 286-95.
Journal code: GLI. ISSN: 0894-1491.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

08/882499

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199411

AB Nerve growth factor (NGF) synthesis was studied with an astroglial cell line derived from rat cerebellar astrocytes by transfection with a simian virus 40 T containing retroviral vector. As in primary astrocytes, NGF synthesis/secretion could be stimulated dose-dependently with interleukin-1 beta (IL-1 beta) and transforming growth factor-beta 1 (TGF-beta 1). We therefore have used this cell line as a model system to analyze putative intracellular signalling pathways underlying the effects of these factors. Protein kinase C inhibitors (calphostin and Ro 31-8830) as well as a lipoxygenase inhibitor (nordihydroguaiaretic acid) did not affect stimulation of NGF synthesis/secretion by IL-1 beta or TGF-beta 1. However, dibutyryl cyclic AMP partly inhibited the stimulation by TGF-beta 1 but did not affect that evoked by IL-1 beta. This finding, together with the fact that IL-1 beta and TGF-beta 1 stimulate NGF production/secretion in an additive manner, indicates that different intracellular signalling pathways are involved in the mediation of IL-1 beta and TGF-beta 1 induced NGF production/secretion.

L37 ANSWER 32 OF 70 MEDLINE

DUPLICATE 11

ACCESSION NUMBER: 94304215 MEDLINE

DOCUMENT NUMBER: 94304215

TITLE: Expression of porcine leukocyte 12-lipoxygenase in a baculovirus/insect cell system and its characterization.

AUTHOR: Reddy R G; Yoshimoto T; Yamamoto S; Funk C D; Marnett L J

CORPORATE SOURCE: A.B. Hancock, Jr., Memorial Laboratory for Cancer Research, Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, Tennessee 37232-0146.

CONTRACT NUMBER: CA47479 (NCI)
ES00267 (NIEHS)

SOURCE: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1994 Jul)
312 (1) 219-26.
Journal code: 6SK. ISSN: 0003-9861.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199410

AB Arachidonate 12-lipoxygenase (12-LO) from porcine leukocytes was expressed in insect cells using a baculovirus expression vector. The recombinant 12-LO was expressed as an N-terminal fusion protein with a 31-amino acid polypeptide carrying a six-histidine tag and an enterokinase cleavage site. Maximal intracellular enzyme activity and protein levels were observed 48 h after infection of Spodoptera

Searcher : Shears 308-4994

frugiperda cells with the recombinant virus. Cells were lysed and the recombinant protein was purified in a single step by Ni²⁺-nitrilotriacetate column chromatography. The purified enzyme migrated as a single band on sodium dodecyl sulfate-polyacryl-amide gel electrophoresis. Recombinant enzyme catalyzed the formation of 12-hydroperoxy-5,8,10,14-eicosatetraenoic acid and a small amount of 15-hydroperoxy-5,8,11,13-eicosatetraenoic acid. Chiral-phase HPLC analysis indicated that the 12-(S) enantiomer was the predominant product. The purified recombinant 12-lipoxygenase oxygenated linoleic acid to about 19% of the extent of oxygenation of arachidonic acid. Nordihydroguaiaretic acid and 5,8,11,14-eicosatetraynoic acid inhibited the recombinant enzyme with IC₅₀'s of 2.2 and 0.06 micM, respectively. Expression of cloned porcine leukocyte 12-LO in S. frugiperda cells and purification by Ni²⁺-nitrilotriacetate chromatography provides a straightforward method for isolation of milligram quantities of this form of 12-LO.

L37 ANSWER 33 OF 70 AIDSLINE

ACCESSION NUMBER: 1995:12992 AIDSLINE

DOCUMENT NUMBER: AIDS-95921601

TITLE: Inhibition of arachidonate metabolism
alters HIV-1 replication and cytopathicity in
monocytes.

AUTHOR: Genis P; Jett M; Franson R; Gentleman H E; Bernton E

CORPORATE SOURCE: Univ. of Nebraska Medical Center, Omaha, NE.

SOURCE: Natl Conf Hum Retroviruses Relat Infect (1st),
(1993). pp. 161.

PUB. COUNTRY: United States

DOCUMENT TYPE: (MEETING ABSTRACTS)

FILE SEGMENT: AIDS

LANGUAGE: English

ENTRY MONTH: 199512

AB The interactions between HIV-1 infected monocytes and astroglia result in eicosanoid production that modulates cytokine and neurotoxic activities from virus-infected monocytes. (Genis, 1992, J. Exp. Med. 176:1703). To investigate the role of eicosanoids in HIV-1 neuropathogenesis, we determined whether arachidonate metabolite inhibitors altered HIV replication. Monocytes purified by centrifugal elutriation were inoculated with HIV-1 ADA at an MOI=1. During the course of infection cells were treated with either nordihydroguaiaretic acid (NDGA), a non-specific lipoxygenase inhibitor, THC-7-oic acid (THC7), a PAF antagonist, indomethacin, a cyclooxygenase inhibitor, or dexamethasone (DEX) or PX-52, both inhibitors of phospholipase A2, at concentrations from 2-100 micromolar. RT activity and syncytia were monitored over a 14 day period. Monocyte viability was confirmed by NBT dye reduction. DEX and NDGA

Searcher : Shears 308-4994

reduced greater than 3-fold HIV replication and virus-induced cytopathicity. Interestingly, indomethacin increased both Rt activity and cytopathicity. THC7 and PX52 had modest effects on HIV production. These data suggest that arachidonate metabolites regulate HIV replication and cytopathicity in monocytes. Inhibitors of these pathways could effect HIV infection in brain macrophages.

L37 ANSWER 34 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS

ACCESSION NUMBER: 1993:431582 BIOSIS

DOCUMENT NUMBER: PREV199396086207

TITLE: Effects of alpha-2- and beta-adrenergic agonism on glucagon secretion from perfused pancreata of normal and streptozocin-induced diabetic rats.

AUTHOR(S): Hirose, Hiroshi (1); Maruyama, Hiroshi; Ito, Katsuhiko; Kido, Koichi; Koyama, Kazunori; Saruta, Takao

CORPORATE SOURCE: (1) Dep. Internal Med., Keio Univ. Sch. Med., 35 Shinanomachi, Shinjuku-ku, Tokyo 160 Japan

SOURCE: Metabolism Clinical and Experimental, (1993) Vol. 42, No. 8, pp. 1072-1076.

ISSN: 0026-0495.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Insulin secretion is known to be inhibited by alpha-2-adrenergic agonism and stimulated by beta-adrenergic agonism in both experimental animals and humans. In contrast, adrenergic regulation of glucagon secretion remains controversial. This study was designed to determine the effects of alpha-2- and beta-adrenergic agonism on islet alpha cells, using isolated perfused pancreata of normal and streptozocin-induced diabetic (STZ-D) rats. The alpha-2-adrenoceptor agonist clonidine at a concentration of 10⁻⁷ mol/L significantly stimulated glucagon secretion as compared with basal levels in both normal (1,286 +- 90 v 417 +- 53 ng/L, P < .01) and STZ-D rats (551 +- 86 v 130 +- 19 ng/L, P < .01). Also, the beta-adrenoceptor agonist isoproterenol at a concentration of 10⁻⁷ mol/L significantly stimulated glucagon secretion as compared with basal levels in both normal (751 +- 130 v 347 +- 41 ng/L, P < .05) and STZ-D rats (182 +- 22 v 92 +- 20 ng/L, P < .01). Furthermore, these alpha-2- and beta-agonistic effects were almost completely inhibited in the presence of the alpha-2-adrenoceptor antagonist yohimbine and the beta-adrenoceptor antagonist propranolol at a concentration of 10⁻⁶ mol/L, respectively. Insulin secretion was markedly reduced in STZ-D rats. These results suggest that even in a severely diabetic state, not only beta- but also alpha-2-adrenergic agonism stimulates glucagon secretion from rat pancreatic alpha cells.

L37 ANSWER 35 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE

ACCESSION NUMBER: 93179288 EMBASE
 DOCUMENT NUMBER: 1993179288
 TITLE: Poly I:C-induced antiviral and cytotoxic activities are mediated by different mechanisms.
 AUTHOR: Pyo S.; Gangemi J.D.; Ghaffar A.; Mayer E.P.
 CORPORATE SOURCE: Dept. of Microbiology/Immunology, University of South Carolina, School of Medicine, Columbia, SC 29208, United States
 SOURCE: International Journal of Immunopharmacology, (1993) 15/4 (477-486).
 ISSN: 0192-0561 CODEN: IJIMDS
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT:
 004 Microbiology
 016 Cancer
 026 Immunology, Serology and Transplantation
 029 Clinical Biochemistry
 030 Pharmacology
 037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Macrophages play an important role in host defenses against tumors and virus infections by killing tumor or virus infected cells (extrinsic cytotoxicity) and by limiting virus replication within themselves (intrinsic antiviral activity). Since common macrophage products may be involved in both extrinsic cytotoxicity and intrinsic antiviral activity, we decided to investigate the mechanisms by which Poly I:C-activated macrophages resist infection with HSV-1 and inhibit the growth of tumor cells. The ability of macrophages to resist infection with HSV-1 or to inhibit growth of tumor cells was assessed following treatment with Poly I:C in the presence of antibodies to various cytokines or in the presence of inhibitors/scavengers of toxic macrophage products. Only antibodies to IFN-.beta. were able to abrogate the protective effects of Poly I:C in macrophages infected with HSV-1, suggesting that the antiviral activity induced by this immunomodulator was mediated by the production of IFN-.beta., which acted in an autocrine manner. In contrast, anti-TNF-.alpha., anti-IFN-.alpha./.beta., anti-IFN-.beta. antibodies and inhibitors of nitric oxide and C1q production were all able to partially abrogate Poly I:C-induced cytostatic activity, suggesting that multiple mechanisms are involved in macrophage cytostasis. Our results indicate the Poly I:C-induced intrinsic antiviral and extrinsic cytotoxic activities are mediated by different mechanisms.

L37 ANSWER 36 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS

ACCESSION NUMBER: 1993:431581 BIOSIS

Searcher : Shears 308-4994

DOCUMENT NUMBER: PREV199396086206
 TITLE: Protection of islet cells from inflammatory cell death in vitro.
 AUTHOR(S): Burkart, V. (1); Kolb, H.
 CORPORATE SOURCE: (1) Diabetes Res. Inst., Auf'm Hennekamp 65, D-40225 Dusseldorf Germany
 SOURCE: Clinical and Experimental Immunology, (1993) Vol. 93, No. 2, pp. 273-278.
 ISSN: 0009-9104.
 DOCUMENT TYPE: Article
 LANGUAGE: English

AB Islet cells cocultured with activated macrophages are lysed within 15 h in vitro. We showed previously that nitric oxide generated by macrophages is a major mediator of islet cell death. We have now probed several pathways to interfere with the chain of events leading to islet cell death. Scavenging of extracellular oxygen radicals by superoxide dismutase and catalase did not improve islet cell survival. Scavenging of extra- and intracellular oxygen radicals by two potent substances, citiolone and dimethyl-thiourea, also did not reduce islet cell lysis, while a lipid-soluble scavenger, probucol, provided partial protection. These findings argue against a synergistic action of nitric oxide and oxygen radicals in islet cell toxicity. The inhibition of poly(ADP-ribose)polymerase by 3-aminobenzamide significantly improved islet cell survival. Selective inhibitors of cyclooxygenase, such as indomethacin or acetylsalicylic acid, did not improve islet cell survival. Full protection was seen in the presence of NDGA, an inhibitor of lipoxygenase, and partial suppression was caused by BW755c, an inhibitor of both lipoxygenase and cyclooxygenase. We conclude that inflammatory islet cell death caused by activated macrophages involves the activation of arachidonic acid metabolism and of poly(ADP-ribose)polymerase, but that scavenging of oxygen free radicals provides little protection from lysis.

L37 ANSWER 37 OF 70 MEDLINE
 ACCESSION NUMBER: 93285336 MEDLINE
 DOCUMENT NUMBER: 93285336
 TITLE: Correlation between phospholipase A2 activity and intra-Golgi protein transport reconstituted in a cell-free system.
 AUTHOR: Tagaya M; Henomatsu N; Yoshimori T; Yamamoto A; Tashiro Y; Fukui T
 CORPORATE SOURCE: Institute of Scientific and Industrial Research, Osaka University, Japan.
 SOURCE: FEBS LETTERS, (1993 Jun 14) 324 (2) 201-4.
 Journal code: EUH. ISSN: 0014-5793.
 PUB. COUNTRY: Netherlands
 Journal; Article; (JOURNAL ARTICLE)
 Searcher : Shears 308-4994

08/882499

LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199309

AB A wide variety of phospholipase A2 inhibitors blocks intra-Golgi protein transport reconstituted in a cell-free system. Phospholipase A2 activity detectable under the protein transport assay conditions is actually inhibited by the inhibitors. There is a good correlation between the inhibition of protein transport and that of phospholipase A2 activity. Prolactin secretion from GH3 cells is also blocked by a membrane-permeable phospholipase A2 inhibitor, suggesting the physiological relevance to inhibition of protein transport in vitro by phospholipase A2 inhibitors.

L37 ANSWER 38 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 93084468 EMBASE
DOCUMENT NUMBER: 1993084468
TITLE: 1992 new drug approvals.
SOURCE: Hospital Formulary, (1993) 28/2 (125-127).
ISSN: 0098-6909 CODEN: HOFOD
COUNTRY: United States
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L37 ANSWER 39 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 93168249 EMBASE
DOCUMENT NUMBER: 1993168249
TITLE: Squamous cell carcinoma of the skin: Will heightened awareness of risk factors slow its increase?.
AUTHOR: Hacker S.M.; Flowers F.P.
CORPORATE SOURCE: Division of Dermatology, Florida University Coll. of Medicine, PO Box 100277, Gainesville, FL 32610-0277, United States
SOURCE: Postgraduate Medicine, (1993) 93/8 (115-126).
ISSN: 0032-5481 CODEN: POMDAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 013 Dermatology and Venereology
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Although squamous cell carcinoma of the skin is still less common than basal cell carcinoma, its incidence is increasing at an alarming rate. Cumulative sun exposure is a major risk factor, and deterioration of the ozone layer combined with life-style choices that promote time in the sun may account for part of the increased

Searcher : Shears 308-4994

incidence. Other risk factors for squamous cell carcinoma include exposure to ionizing radiation, arsenic, or industrial chemicals; viral infection; preexisting burns and scars; and immunosuppression. Actinic keratosis is considered a precancerous lesion that should be watched closely. Treatment methods for squamous cell carcinoma vary depending on the size and location of the lesion. Knowledge of high-risk locations and appropriate treatment choices ensures proper care and decreases the likelihood of metastasis.

L37 ANSWER 40 OF 70 MEDLINE

DUPLICATE 13

ACCESSION NUMBER: 93287009 MEDLINE

DOCUMENT NUMBER: 93287009

TITLE: Immunomodulation of cellular cytotoxicity to herpes simplex virus infection in pregnancy by inhibition of eicosanoid metabolism.

AUTHOR: Feinberg B B; Tan N S; Donovan P K; Loftin K C; Gonik B

CORPORATE SOURCE: Department of Obstetrics, Gynecology and Reproductive Sciences, University of Texas Medical School, Houston.

SOURCE: JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1993 Mar) 23 (2) 109-18.

Journal code: JWS. ISSN: 0165-0378.

PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199309

AB In an effort to evaluate the relationships among pregnancy, cellular cytotoxicity and herpes simplex virus (HSV) infection, we conducted a series of experiments investigating: (1) the maternal cellular cytotoxic response to HSV infection as compared with non-pregnant hosts, (2) the influence of both cyclooxygenase and lipoxygenase products on cytotoxicity by selective inhibition of their metabolic pathways, and (3) the potential pregnancy-related differences in immune response to selective inhibition of eicosanoid metabolism. Indomethacin was used for cyclooxygenase blockade and nordihydroguaiaretic acid was used to evaluate lipoxygenase inhibition. In the non-infected animals no differences in cytotoxicity were observed between pregnant (1.5% +/- 0.7%) and non-pregnant (4.6% +/- 2.0%) groups. HSV infection increased cytotoxicity equally in both groups (pregnant: 10.6% +/- 2.0% vs. non-pregnant: 14.2% +/- 3.4%). Indomethacin did not significantly alter cytotoxicity in either the pregnant or the non-pregnant groups compared with controls (12.8% +/- 1.8% vs. 10.6% +/- 2.0% and 14.3% +/- 3.9% vs. 14.2% +/- 3.4%, respectively). In

Searcher : Shears 308-4994

08/882499

contrast, NDGA elicited a significant reduction in the cytotoxic response in both pregnant and non-pregnant hosts (6.2% +/- 1.1% vs. 10.6% +/- 2.0% and 5.7% +/- 1.1% vs. 14.2% +/- 3.4%, respectively). From our study we conclude that: (1) cytotoxicity is maintained at low levels in the absence of HSV infection, (2) HSV infection induces a significant augmentation in host cellular cytotoxicity, (3) pregnant and non-pregnant cytotoxic responses to HSV infection appear comparable, (4) indomethacin does not augment in vitro cytotoxicity to HSV infection and (5) NDGA suppresses cytotoxicity, providing evidence that lipoxygenase metabolites are essential to cytotoxic cell function.

L37 ANSWER 41 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 93120951 EMBASE

DOCUMENT NUMBER: 1993120951

TITLE: 1992 drug approvals: The year in review.

AUTHOR: Estrada J.

SOURCE: Drug Therapy, (1993) 23/3 (55-58+63).

ISSN: 0001-7094 CODEN: DRTHE2

COUNTRY: United States

DOCUMENT TYPE: Journal; Note

FILE SEGMENT: 030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Twenty-six new molecular entities were approved by the FDA in 1992. Several of them were the first in new classes of drugs to reach the market. Other firsts included the first joint review of a drug by the FDA and the Canadian Health Protection Branch and the availability of a once-daily NSAID and a once-daily quinolone antibiotic. Consumers are keeping their eyes on finasteride, the first nonsurgical treatment for benign prostatic hyperplasia, and sumatriptan, a promising new migraine remedy. Several drugs of interest to AIDS patients were also approved. Following is a brief summary of information about each new entity approved in 1992.

L37 ANSWER 42 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 93058339 EMBASE

DOCUMENT NUMBER: 1993058339

TITLE: P and T update: New approvals and dosage forms.

SOURCE: Hospital Formulary, (1993) 28/1 (7-8+13).

ISSN: 0098-6909 CODEN: HOFOD

COUNTRY: United States

DOCUMENT TYPE: Journal; Note

FILE SEGMENT: 030 Pharmacology

037 Drug Literature Index

Searcher : Shears 308-4994

038 Adverse Reactions Titles

LANGUAGE: English.

L37 ANSWER 43 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS

ACCESSION NUMBER: 1993:74237 BIOSIS

DOCUMENT NUMBER: PREV199395038737

TITLE: Redox status of cells influences constitutive or induced NF-kappa-B translocation and HIV long terminal repeat activity in human T and monocytic cell lines.

AUTHOR(S): Israel, Nicole (1); Gougerot-Pocidalo, Marie-Anne; Aillet, Fabienne; Virelizier, Jean-Louis

CORPORATE SOURCE: (1) Unite d'Immunologie Virale, Inst. Pasteur, 75724 Paris Cedex 15 France

SOURCE: Journal of Immunology, (1992) Vol. 149, No. 10, pp. 3386-3393.

ISSN: 0022-1767.

DOCUMENT TYPE: Article

LANGUAGE: English

AB We have tested the hypothesis that cellular activation events occurred in T lymphocytes and monocyte and mediated through translocation of the transcription factor NF-kappa-B are dependent upon the constitutive redox status of these cells. We used phenolic, lipid-soluble, chain-breaking antioxidants butylated hydroxyanisole (BHA), nordihydroquaiaretic acid, or alpha-tocopherol (vitamin E) to show that peroxyl radical scavenging in unstimulated and PMA- or TNF-stimulated cell blocks the functions depending on NF-kappa-B activation. BHA was found to suppress not only PMA- or TNF-induced, but also constitutive. HIV-enhancer activity concomitant to an inhibition of NF-kappa-B binding activity in both lymphoblastoid T (J.Jhan) and monocytic (U937) cell lines. This was also true for KBF (p50 homodimer) binding activity in U937 cells. Secretion of TNF, the product of another NF-kappa-B dependent gene, was abolished by BHA in PMA-stimulated U937 cells. The anti-oxidative effect of BHA was accompanied by an increase in thiol, but not glutathione, content in stimulated and unstimulated T cells, whereas TNF stimulation itself barely modified the cellular thiol level. Oxidative stress obtained by the addition of H-20-2 to the culture medium of J.Jhan or U937 cells could not by itself induce NF-kappa-B activation. These observations suggest that TNF and PMA did not lead to NF-kappa-B activation through induction of changes in the cell redox status. Rather, TNF and PMA can exert their effect only if cells are in an appropriate redox status, because prior modification toward reduction with BHA treatment prevents this activation. It appears that a basal redox equilibrium tending toward oxidation is a prerequisite for full activation of transduction pathways regulating the activity of NF-kappa-B-dependent genes.

L37 ANSWER 44 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1992:261701 BIOSIS
DOCUMENT NUMBER: BA93:138026
TITLE: DIETHYLDITHIOCARBAMATE DITHIOCARB SODIUM EFFECT ON ARACHIDONIC ACID METABOLISM IN HUMAN MONONUCLEAR CELLS GLUTATHIONE PEROXIDASE-LIKE ACTIVITY.
AUTHOR(S): HOSNI M; MESKINI N; PRIGENT A-F; ANKER G; JOULAIN C; EL HABIB R; LAGARDE M
CORPORATE SOURCE: INSERM UNITE 205, LABORATOIRE CHIMIE BIOLOGIQUE, BAT. 406, INSTITUT NATIONAL SCIENCES APPLIQUEES DE LYON, 20 AVENUE A. EINSTEIN, 69621 VILLEURBANNE, FR.
SOURCE: BIOCHEM PHARMACOL, (1992) 43 (6), 1319-1329.
CODEN: BCPA6. ISSN: 0006-2952.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Diethyldithiocarbamate (DTC), a thiol delivery agent, has been shown to significantly reduce the frequency of primary opportunistic infections in HIV-infected patients. This therapeutic effect has been related to the capacity of DTC to reverse the deleterious effects of the oxidative stress occurring in HIV infection. The influence of DTC on the oxygenated metabolism of arachidonic acid (AA) was investigated in mitogen-stimulated human peripheral blood mononuclear cells (PBMC). Upon incubation with PBMC previously labelled with [³H]AA, Concanavalin A (Con A) markedly increased cyclooxygenase and lipoxygenase activities, within 30 min, as judged by thromboxane B₂ (TxB₂) and hydroxyeicosatetraenoic acid (HETE) production. Con A activation of [³H]AA platelets also increased 12-HETE production but did not induce any TxB₂ synthesis. Micromolar concentrations of DTC, added simultaneously with the mitogen, significantly enhanced the synthesis of HETEs above the Con A-induced level while TxB₂-induced synthesis was inhibited but only at DTC concentrations higher than 50 .mu.M. In the presence of nordihydroguaiaretic acid, a lipoxygenase inhibitor, which inhibited the Con A-induced synthesis of HETEs by 78%, DTC no longer stimulated HETE production above the Con A-induced level. Reverse phase HPLC analysis showed that Con A increased the PBMC production of 5-, 12- and 15-HETEs. In the presence of 5 .mu.M DTC, 5-HETE production was entirely suppressed whereas the 15-HETE level was markedly enhanced, 12-HETE production by the contaminating platelets remained unchanged. In vitro experiments indicated that DTC alone did not significantly influence 15-hydroperoxyeicosatetraenoic (15-HPETE) production by the soybean 15-lipoxygenase but, in the presence of added reduced glutathione, DTC markedly reduced 15-HPETE into 15-HETE. In addition, DTC was able to substitute for cellular extract in the glutathione peroxidase (GPx) assay system. Taken together, these results indicate that DTC, through its "GPx-like" activity is able to modify the lipoxygenase cascade. Its ability to selectively reduce 15-HPETE known to stimulate immunosuppressive

Searcher : Shears 308-4994

08/882499

T-cells might help to explain its positive regulatory effect upon the immune system.

L37 ANSWER 45 OF 70 MEDLINE

DUPPLICATE 14

ACCESSION NUMBER: 92405734 MEDLINE

DOCUMENT NUMBER: 92405734

TITLE: Stimulation of receptor-coupled phospholipase A2 by interferon-gamma.

AUTHOR: Ponzoni M; Montaldo P G; Cornaglia-Ferraris P

CORPORATE SOURCE: Pediatric Oncology Research Laboratory, G. Gaslini Children's Hospital, Genoa, Italy.

SOURCE: FEBS LETTERS, (1992 Sep 21) 310 (1) 17-21.
Journal code: EUH. ISSN: 0014-5793.

PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199212

AB The biomolecular mechanisms that mediate signal transduction by type II (gamma) interferon (IFN) are poorly understood. IFN-gamma is a potent growth inhibitory cytokine also endowed with antiviral, immunomodulatory, and differentiating activities on various cell targets, including neural cells. IFN-gamma induced a rapid and transient activation of phospholipase A2 in LAN-5, a human neuroblastoma cell line. A consequence of phospholipase A2 activation was the release of arachidonic acid and the generation of lysophospholipids from membrane phospholipids. Treatment of pre-labeled LAN-5 cells with a receptor-saturating concentration of IFN-gamma led to a time-dependent release of [3H]arachidonic acid into the culture media and generation of [32P]lysophatidylcholine. Pretreatment of cultures with the phospholipase A2 inhibitor, bromophenacyl bromide, markedly inhibited both [3H]arachidonic acid release and lysophatidylcholine production induced by IFN-gamma treatment. Pretreatment of LAN-5 cells with nordihydroguaiaretic acid, a lipoxygenase inhibitor, or with indomethacin, a cyclooxygenase inhibitor, amplified the release of [3H]arachidonic acid and production of lysophatidylcholine induced by non-saturating concentrations of IFN-gamma. In parallel, and with the same time-dependent effect, a significant decrease in phosphatidylcholine labeling was observed in IFN-gamma-treated cells, further indicating that a potential signal transduction mechanism of IFN-gamma is the hydrolysis of membrane phosphatidylcholine by phospholipase A2.

L37 ANSWER 46 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD

ACCESSION NUMBER: 92-46813 DRUGU M P E

TITLE: Biological Activities and Mechanisms of Action of PGJ2 and Related Compounds: an Update.

Searcher : Shears 308-4994

AUTHOR: Fukushima M
 LOCATION: Nagoya, Japan
 SOURCE: Prostaglandins Leukotrienes Essent. Fatty Acids (47, No. 1, 1-12, 1992) 3 Fig. 124 Ref.
 CODEN: PLEAEU ISSN: 0952-3278
 AVAIL. OF DOC.: Department of Internal Medicine, Aiichi Cancer Center, Chikusa-ku, Nagoya 464, Japan.
 LANGUAGE: English
 DOCUMENT TYPE: Journal
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature
 AN 92-46813 DRUGU M P E
 AB Recent advances in the biological activity and mechanism of action of PGJ2 and related compounds is reviewed. Effects on cell division, binding to fatty acid binding proteins, involvement in heat shock, antiviral activity, stimulation of osteogenesis, inflammatory activity, antiproliferative activity and in-vivo antitumor activity in animals are discussed. Further studies may discern the common vulnerability of malignant cells and may provide a new chemotherapeutic strategy.
 ABEX The chemistry of alkylidene cyclopentenone PG is detailed (with reference to delta-7-PGA1, clavulone-1, punaglandin-3, TEI-3313). The natural occurrence of delta-12-PGJ2 is discussed. Cyclopentenone and alkylidene cyclopentenone PG disturb membrane integrated systems including precursor uptake, adenylate cyclase, Ca-stimulated ATPase and calmodulin-dependent guanylate cyclase. Gamma-glutamyl-cysteine synthetase is induced by cyclopentenone PG. The involvement of cyclopentenone PG in heat shock is detailed; the cellular response to cyclopentenone PG is similar to that induced by arsenite. The antiviral activity of PG including PGAl and 16,16-dimethyl-PGQ2-methylester is detailed. Delta-12-PGJ2 and TEI-3313 have activity similar to L-alpha-25-dihydroxyvitamin D3 in stimulating osteogenesis. The inflammatory effects of PGJ2 are compared with 9alpha,11beta-PGF2, BN24SC, and PGD2. Antiproliferative effects of PG (e.g. delta-7-PGA1, delta-12-PGJ2, OP-41483, 11-HETE, misoprostol) have been demonstrated in various cells (endometrial carcinoma, ML-1, HL-60, U-937, ovarian carcinoma, human glioma) effects of ketoprofen, NDGA, AA-863, U-60257 (piriprost), AA-861 (docebenone), quercetin, 5-HETE, cisplatin, doxorubicin, and l-phenylalanine mustard are also detailed. I.p. delta-12-PGJ2 suppresses the growth of human colon cancer in mice. Delta-7-PGA1 and TEI-0303 suppress VX-2 tumor growth in rabbits. Future perspectives are detailed. Evaluation of an adjuvant effect of delta-7-PGA1 to cisplatin and synergistic effects of delta-12-PGJ2 and tumor necrosis factor may help develop a new concept of chemotherapy.
 (E35/LJ)

08/882499

ACCESSION NUMBER: 91082447 MEDLINE
DOCUMENT NUMBER: 91082447
TITLE: Inhibitors of the lipoxygenase pathway
specifically block orthopoxvirus replication.
AUTHOR: Palumbo G J; Buller R M
CORPORATE SOURCE: Laboratory of Viral Diseases, National Institute of
Allergy and Infectious Diseases, National Institutes
of Health, Bethesda, Maryland 20892.
SOURCE: VIROLOGY, (1991 Jan) 180 (1) 457-63.
Journal code: XEA. ISSN: 0042-6822.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199104

AB Inhibitors of arachidonic acid metabolism,
5,8,11,14-eicosatetraynoic acid (ETYA), BW755c, and
nordihydroguaiaretic acid were found to specifically
interfere with the replication of cowpox virus (an
orthopoxvirus) both in vivo and in vitro. Further studies in vitro
showed that the drugs ETYA and BW755c were effective in
inhibiting the replication of two additional
orthopoxviruses, ectromelia and vaccinia viruses, but not
human parainfluenza virus-3. In ETYA-treated and
cowpox virus-infected cells, early and late gene
expression were near normal levels, whereas the assembly of
virus-specific membranes was severely reduced. These results
are compatible with a model of orthopoxvirus replication that has an
obligate requirement for arachidonic acid or one of its metabolic
forms, possibly in the assembly of virus-specific
membranes.

L37 ANSWER 48 OF 70 PROMT COPYRIGHT 1999 IAC

ACCESSION NUMBER: 91:196515 PROMT
TITLE: IN THE PUBLIC EYE: Media Exaggerates Benefits of
Laser Therapy, Some Contend
SOURCE: Dermatology Times, (Apr 1991) pp. 36.
ISSN: 0196-6197.
LANGUAGE: English
WORD COUNT: 893

FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB This monthly column contains abstracts of articles from consumer
publications on topics relevant to dermatology. By being alerted to
articles appearing in the lay press, you may be better prepared to
answer questions, correct erroneous or misinterpreted information,
offer patients easy-to-read discussions of dermatology and skin
care, and become attuned to how the media cover dermatologic issues.
Health (February 1991)

Searcher : Shears 308-4994

08/882499

"The benefits of lasers are being hyped by overly optimistic news reports, a public enthralled with the instruments' novelty, and competitive physicians, hospitals, and laser companies eager to cash in on the devices' high-tech image." This atmosphere lends a premature air of validity to some laser treatments, some contend. The primary example cited was a case of permanent dot scarring as a result of spider vein laser treatment.

Many doctors believe that lasers should only be used when clinical trials have demonstrated a significant advantage over traditional techniques. Consistently successful laser treatment of spider veins, for instance, has not been demonstrated, but Q-switched ruby laser tattoo removal has been clearly established. The American Society of Plastic and Reconstructive Surgeons (ASPRS) ... issued a statement warning the public about "potential risks and drawbacks of certain experimental laser procedures."

Mademoiselle (March 1991)

Stress can trigger an imbalance in the endocrine system and weaken the immune system, leading to various skin disorders, such as canker sores, cold sores, and acne. Cold sores are highly contagious viral infections.

By Tom Celebrezze

THIS IS AN EXCERPT: Copyright 1991 Edgell Communications, Inc.

L37 ANSWER 49 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1990-336689 [45] WPIDS
DOC. NO. CPI: C90-146074
TITLE: Use of arachidonic acid or its analogue - for
treatment of cytokine mediated diseases
e.g. common cold or influenza.
DERWENT CLASS: B02 B05
INVENTOR(S): LIM, L; TAN, Y H
PATENT ASSIGNEE(S): (UYSI-N) NAT UNIV OF SINGAPORE; (TANY-I) TAN Y H
COUNTRY COUNT: 7
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 396251	A	901107	(9045)*		
	R:	CH DE FR GB LI NL			
JP 03083933	A	910409	(9120)		
EP 396251	A3	920708	(9334)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 396251	A	EP 90-303361	900329
JP 03083933	A	JP 89-220144	890825
EP 396251	A3	EP 90-303361	900329
		Searcher : Shears	308-4994

PRIORITY APPLN. INFO: GB 89-7308 890331; JP 89-220144 890825

AN 1990-336689 [45] WPIDS

AB EP 396251 A UPAB: 19931119

Specific cytokines are type I and II interferon. Inhibition of at least 50% is achieved. Compounds of use in this invention are monocarboxylic polyunsaturated fatty acids, their salts, 1-4C alkyl esters, amides and 1-4C alkylamides. Fatty acids have 14 to 24 carbon atoms most preferably 20. Suitable compounds include 5, 11, 14-eicosatetraenoic acid (arachidonic); 5, 8, 11, 14-eicosatetraynoic acid; 5,8,11-eicosatriynoic acid, linoleic acid and their derivatives. Other compounds are ketoconazole, nordihydroguaiaretic acid and quercetin. The compositions may be in the form of nasal drops, a nasal spray, a balm, cream or tablets. Dosage is 0.5 to 150 mg of arachidonic acid or analogue per dose when administered orally.

USE/ADVANTAGE - The compounds of the invention interfere with binding of ligands such as cytokines to cellular receptors and so inhibit the action of interferon on cells after an antiviral state has been established. They are therefore used to treat viral diseases especially the common cold or flu. @ (17pp Dwg.No.0/7)

0/7

L37 ANSWER 50 OF 70 TOXLIT

ACCESSION NUMBER: 1991:31002 TOXLIT

DOCUMENT NUMBER: CA-114-115083U

TITLE: Use of fatty acids or other compounds for the treatment of diseases associated with cytokines, such as alleviation of symptoms of influenza or the common cold.

AUTHOR: Tan YH; Lim L

SOURCE: (1990). Eur. Pat. Appl. PATENT NO. 396251 11/07/90
(National University of Singapore).

PUB. COUNTRY: Singapore

DOCUMENT TYPE: Patent

FILE SEGMENT: CA

LANGUAGE: English

OTHER SOURCE: CA 114:115083

ENTRY MONTH: 199106

AB Arachidonic acid (I), an arachidonic acid analog, nordihydroguaiaretic acid (II), ketoconazole (III), or quercetin or used in the prepn. of a medicament for use in the treatment of a disease state assocd. with the endogenous presence and/or prodn. of a cytokine. The compds. of the invention can be used to alleviate the symptoms of the common cold or influenza. Thus, 50 muM I, 50 muM II, and 100 muM III inhibited the antiviral state induced by alpha- or

Searcher : Shears 308-4994

08/882499

beta-interferon by .gtoreq.90%; 50 muM I also inhibited the antiviral state induced by gamma-interferon by .gtoreq.80%. Data are presented that suggest that I and other compds. of the invention can diminish the binding of ligands (interferon) to their receptors.

L37 ANSWER 51 OF 70 TOXLINE

ACCESSION NUMBER: 1991:13243 TOXLINE

DOCUMENT NUMBER: BIOSIS-91-00245

TITLE: Staphylococcal enterotoxin A induced interferon (IFN)-gamma production in spleen cells from BCG-immunized mice: The IFN production is dependent on leukotriene C4 but not dependent on interleukin 2.

AUTHOR: KATO K; SHIROSITA K; KUROSAWA S; MIZUKOSHI N; YAMAMOTO K-I; AZUMA I; OKUYAMA H; NISHIHARA J

CORPORATE SOURCE: Dep. Intern. Med., Tomakomai City General Hosp., 1-2-21 Honkou-chyo, Tomakomai 053, Japan.

SOURCE: IMMUNOBIOLOGY, (1990). Vol. 181, No. 1, pp. 40-50.
CODEN: IMMND4.

FILE SEGMENT: BIOSIS

LANGUAGE: English

ENTRY MONTH: 199102

AB BIOSIS COPYRIGHT: BIOL ABS. In our previous paper, we showed that IFN was induced in sera by injection of staphylococcal enterotoxin A (SEA) in Bacillus Calmette-Guerin (BCG) immunized C57BL/6 (B6) mice. In analyzing the phenomenon in vitro, we showed that SEA induced IFN-gamma in the supernatant of the spleen cell culture from BCG immunized B6 mice and that leukotriene C4 (LTC4) from BCG activated macrophages in the spleen was involved in the IFN production from Ly 1+ T cells. On the other hand, interleukin-2 (IL-2) has reported to play an important role in the regulation of synthesis of IFN-gamma by T cells. In the present study, we examined whether IL-2 is involved in SEA-induced IFN production. The result showed that the SEA-induced IFN-gamma production was observed in spite of suppression of SEA-induced IL-2 production in spleen cells from BCG-immunized B6 mice. On the contrary, the depressed IFN production was observed in spite of high SEA-induced IL-2 production in spleen cells from their control mice. On other hand, LTC4 production was 8 times higher in spleen cells from BCG-immunized B6 mice, high producer of SEA-induced IFN, than in that from BCG-immunized C3H mice, the low producer. We also observed that the IFN and the LTC4 production of spleen cells from BCG-immunized B6 mice was suppressed in the presence of caffeic acid and nordihydroguaiaretic acid, non-specific lipoxygenase inhibitors, and that LTC4 augmented the IFN production of normal B6 mouse spleen cells in the presence of 2-mercaptoethanol. Therefore, involvement of LTC4 rather than of IL-2 was supported in our experimental system.

L37 ANSWER 52 OF 70 MEDLINE

DUPLICATE 16

ACCESSION NUMBER: 90002927 MEDLINE

DOCUMENT NUMBER: 90002927

TITLE: Mechanism of selective killing by dilinoleoylglycerol
of cells transformed by the E1A gene of adenovirus
type 12.AUTHOR: Matsuzaki A; Shimura H; Okuda A; Ohtsu M; Sasaki M;
Onodera K; Kimura GCORPORATE SOURCE: Department of Virology, Kyushu University, Fukuoka,
Japan.SOURCE: CANCER RESEARCH, (1989 Oct 15) 49 (20) 5702-7.
Journal code: CNF. ISSN: 0008-5472.PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199001

AB Rat 3Y1 fibroblasts transformed by the E1A gene of adenovirus type 12 (E1A-3Y1 cells) are highly sensitive to the cell-killing effect of 1,3-dilinoleoylglycerol (DLG) administered in a culture medium, whereas the parental 3Y1 cells are less sensitive (H. Shimura et al., Cancer Res., 48: 578-583, 1988). The selective cytotoxicity of DLG to E1A-3Y1 cells was markedly reduced by the simultaneous administration of nonspecific antioxidants such as vitamin E, butylated hydroxytoluene, and ascorbic acid. Specific scavengers for oxygen radicals had no effect. Lipoxygenase inhibitors (nordihydroguaiaretic acid, esculetin, and baicalein) reduced the DLG-mediated selective cytotoxicity, whereas cyclooxygenase inhibitors (acetylsalicylic acid and indomethacin) showed no effect. The intracellular and extracellular contents of the products from lipid peroxidation as measured by the thiobarbituric acid test were significantly greater in E1A-3Y1 cells than in the parental 3Y1 cells. In comparison with DLG, linoleic acid and monolinoleoylglycerol were equally toxic to E1A-3Y1 and parental 3Y1, and trilinoleoylglycerol was weakly toxic to both types of cells. Scanning electron microscopy revealed that numerous holes about 0.2 micron in diameter were scattered all over the surface of the E1A-3Y1 cells after treating the cultures with DLG. These results suggest that; (a) the DLG-mediated cytotoxicity to the E1A-transformed cells is attributable to lipid peroxidation; (b) the structural property of DLG is essential to the E1A specificity of cytotoxicity; and finally (c) the destruction of the cell membrane is the basis of cytotoxicity of DLG.

L37 ANSWER 53 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD

ACCESSION NUMBER: 89-44753 DRUGU T P

TITLE: Phytohemagglutinin Mitogenic Response of Normal
Individuals Vaccinated with Hepatitis B Vaccine.AUTHOR: Filion L G; Saginur R; Izaguirre C A
Searcher : Shears 308-4994

08/882499

LOCATION: Ottawa, Ontario, Canada
SOURCE: J.Infect.Dis. (160, No. 3, 398-404, 1989) 4 Fig. 3 Tab.
15 Ref.

CODEN: JIDIAQ ISSN: 0022-1899

AVAIL. OF DOC.: Department of Microbiology and Immunology, Faculty of Medicine, University of Ottawa, Ontario, K1H 8M5, Canada.

LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AN 89-44753 DRUGU T P

AB In 34 healthy people vaccinated i.m. with Hepatitis-B-vaccine (Heptavax B, HB, Merck-Frosst), the PHA response was suppressed 2 day after the first dose but not after subsequent doses. The PHA blastogenic response on day 7 was not enhanced by interleukin-2 (IL-2, Genzyme, USA) or indometacin (IN, Sigma-Chem.) though more cells expressed CD25 in their presence. Removal of CD4+ or CD8+ cells enhanced the PHA response on days 2 and 4 only. Addition of IL-2 alone or with PHA did not reverse the suppression at any time tested. In vitro suppressor cell induction was blocked by addition of IN at the time of culture initiation. Addition of IN or nordihydroguaiaretate to control cultures did not affect their response to PHA.

ABEX Methods The 13 males (mean age 30 yr, range 22-50 yr) and 21 females (mean age 27 yr, range 22-40 yr) were injected with 20 ug of HB in the deltoid muscle on days 0, 28 and 180. Results The blastogenic response to PHA was suppressed by about 33% on day 2 after vaccination but recovered by day 21. There was a significant increase in CD25 levels after the first HB dose which peaked on day 21. CD25 levels were significantly increased after each subsequent vaccination, reaching a maximum of 14% of peripheral blood mononuclear cells by day 187. The PHA response was boosted about 2-fold by the elimination of CD4+ or CD8+ cells from donors on days 2 and 4. At all other sampling times, the removal of these lymphocytes and especially CD4+ cells decreased the PHA blastogenic response. In vitro, cells needed to be incubated with HB for 3 days or more before stimulation with PHA in order to achieve effective suppression of the blastogenic response. (W137/LJ)

L37 ANSWER 54 OF 70 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 89198836 MEDLINE
DOCUMENT NUMBER: 89198836
TITLE: Reversal of virus-induced alveolar
macrophage bactericidal dysfunction by cyclooxygenase
inhibition in vitro.
AUTHOR: Laegreid W W; Liggitt H D; Silflow R M; Evermann J R;
Searcher : Shears 308-4994

08/882499

CORPORATE SOURCE: Taylor S M; Leid R W
Department of Veterinary Microbiology, Washington
State University, Pullman 99164-7040.

SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1989 Apr) 45 (4)
293-300.
Journal code: IYW. ISSN: 0741-5400.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198907

AB Virus infection of alveolar macrophages (AM) both in vivo and in vitro has been associated with a decreased ability of these cells to kill bacteria, together with enhanced production of metabolites of arachidonic acid. These metabolites, especially PGE2, may be inhibitory to some phagocyte functions. Primary cultures of bovine AM obtained by bronchoalveolar lavage of normal cattle were infected in vitro with parainfluenza-3 (PI3 virus) virus. Killing of *Staphylococcus epidermidis* by AM was determined on days 1-4 post-infection (p.i.). PI3 virus-infected AM killed significantly fewer bacteria on day 4 p.i. compared to uninfected controls ($12.1 +/ - 1.3\%$ infected vs. $52.7 +/ - 7.2\%$ controls, P less than or equal to 0.05). Bacterial killing by virus-infected AM, but not control AM, was significantly enhanced on day 4 p.i. by addition of cyclooxygenase inhibitors 1 hr prior to bactericidal assay ($28.0 +/ - 4.5\%$ indomethacin, $36.0 +/ - 4.1\%$ mefenamic acid, $38.6 +/ - 7.3\%$ piroxicam, $37.0 +/ - 6.4\%$ NDGA, $44.9 +/ - 7.7\%$ ETYA, P less than or equal to 0.05). Phagocytosis of opsonized sheep erythrocytes and superoxide generation by virus-infected AM were not significantly increased by cyclooxygenase inhibition. Phagosome-lysosome fusion was severely impaired in virus-infected AM. Pretreatment of virus-infected AM with indomethacin significantly enhanced the percentage of cell expressing fusion activity. This data suggests that in vitro bactericidal dysfunction associated with virus infection of AM is partially the result of enhanced production of prostaglandins or thromboxane by AM and/or an abnormal response to normal levels of endogenously produced cyclooxygenase metabolites. The data further indicate the presence of cyclooxygenase sensitive (phagosome-lysosome fusion) and insensitive (phagocytic) components of virus-induced bactericidal dysfunction in AM.

L37 ANSWER 55 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 89-15254 DRUGU T E
TITLE: Topical Nordihydroguaiaretic Acid (NDGA) in Psoriasis.
AUTHOR: Newton J A; Boodle K M; Barr R; Dowd P M; Greaves M W
LOCATION: London, United Kingdom
Searcher : Shears 308-4994

08/882499

SOURCE: Br.J.Dermatol. (120, No. 2, 286-87, 1989) 1 Tab. 3 Ref.

CODEN: BJDEAZ ISSN: 0366-2845

AVAIL. OF DOC.: Institute of Dermatology, UMDS Guy's and St. Thomas',
Lisle St, London WC2, England.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 89-15254 DRUGU T E

AB The clinical and pharmacological effects of NDGA applied topically were evaluated in 10 patients with stable plaque psoriasis. No clinical response was observed and no effect on LTB4 production was demonstrated by a chemokinesis bioassay or HPLC. A positive control treated with 0.025% betamethasone 17-valerate (BM) responded to treatment. (congress abstract).

ABEX 4 Patients with stable plaque psoriasis were initially studied.

NDGA was applied topically using a limiting grid for 14 days. The NDGA was applied in methylated spirit in concentrations ranging from 0.5%-3%. No clinical effect of NDGA was seen although a positive control treated simultaneously with 0.025% BM ointment responded to treatment. A further 6 patients with psoriasis were, therefore, recruited. A large plaque was selected. Diameter circles of 3 x 2 cm were marked, each at least 4 cm apart. The 1st was left untreated, the 2nd was treated daily with a 3% solution (100 ul solution) of NDGA in methylated spirit under occlusion and the 3rd was treated identically, with solvent alone. 1 Patient was withdrawn at 5 days because she developed a viral infection. In the other 5, the clinical response was assessed and chamber fluid was collected after abrasion for the assay of LTB4 using HPLC and a chemokinesis assay. Again, no clinical response was demonstrated. Levels of LTB4/chamber were: 28 +/- 11, 22 +/- 8 and 19 +/- 8 pg in NDGA-, solvent- and untreated skin. (E54/RSV)

L37 ANSWER 56 OF 70 PROMT COPYRIGHT 1999 IAC

ACCESSION NUMBER: 90:463861 PROMT

TITLE: Chemex Pharmaceuticals - Research & Development
Outlays

SOURCE: Annual Report, (1989) pp. 0.

LANGUAGE: English

AB 4. Yale University-The Company has two research contracts with the Yale University Department of Dermatology. Due to financial constraints, the Company has notified the University that it will terminate the general research contract at the end of the termination notice period, September 30, 1990. Chemex will continue to fund the Yale research contract for the development of

Searcher : Shears 308-4994

08/882499

Oligonucleotide Directed Photochemotherapy. ONDP technology was discovered by Yale in 1988 and is owned by Chemex. The ONDP procedure, for which patents have been applied, is being investigated as a potential new treatment of inflammatory, immune and viral skin diseases. The termination of one of the two Yale contracts will reduce by one-half the Company's Yale research costs after September 30, 1990.

5. Other Projects-In addition to projects discussed above, financial resources permitting, the Company will advance development work on methotrexate, cytarabine, and CHX 108 for the potential treatment of psoriasis, viral warts, and dermatitis, respectively.

6. Withdrawal of INDs-For business and/or scientific reasons, Chemex has decided to suspend further development work on the following projects and has withdrawn relevant IND filings on these compounds only for the following potential treatments: NDGA (CHX 100) for psoriasis; spectinomycin (CHX 3101) for acne; amlexanox (CHX 3673) for psoriasis; propoxytane (CHX 107) for psoriasis; and CHX 3988 (Takeda PAF antagonist) for eczema.

L37 ANSWER 57 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1988-161515 [23] WPIDS
DOC. NO. CPI: C88-072034
TITLE: Antitumour compsn. contg. organic cpd. e.g. 1,4-di phenyl-butane deriv - esp. with metal salt potentiator such as zinc chloride, also with antimicrobial and other activities.
DERWENT CLASS: B05 C03
INVENTOR(S): ALLEN, L M; JORDAN, R T
PATENT ASSIGNEE(S): (CHEM-N) CHEMEX PHARM INC
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8803805	A	880602	(8823)*	EN	130
RW:	AT BE CH DE FR GB IT LU NL SE				
W:	AU DK FI JP KP KR NO SU				
AU 8767794	A	880616	(8836)		
EP 290442	A	881117	(8846)	EN	
R:	AT BE CH DE FR GB IT LI LU NL SE				
JP 01501791 W		890622	(8931)		
AU 9168662	A	910314	(9118)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8803805	A	WO 86-US2547	861119
		Searcher : Shears	308-4994

08/882499

EP 290442 A
JP 01501791 W

EP 86-900420 861119
JP 86-500359 861119

PRIORITY APPLN. INFO: WO 86-US2547 861119

AN 1988-161515 [23] WPIDS

AB WO 8803805 A UPAB: 19930923

Antitumour compsns. contain (1) a metal salt potentiator and (2) an organic component. Alternatively, they may contain only certain of the organic components, i.e. 3- or 4-tert.butylphenol; p-hydroxycinnamic acid; norisoguaiacin; d,l-nordihydroguaiaretic acid (NDGA); 1-(3,4-diacetoxyphenyl)-4-phenylbuta-1,3-diene; 1,4-bis(3,4-dihydroxyphenethyl) benzene; alpha,omega-(7-14C)dicarboxylic acids or their salts.

The compsns. pref. contain a salt of Zn, Cr (III), Y, Co (II), Co (III), Ni, Mg, Al, Cu (I), Cu (II), Fe (III), Cd, Sb, Hg, Rb, V or other rare earth metals, and a typical organic cpd. is a catechol butane of formula (I). R₁ and R₂ = H; 1-12C alkyl, alkenyl, alkoxy or alkenyloxy; (CO)_n(CH₂)_m(CO₂)pRa; glycoside residues (opt. with hydroxy H replaced by 1-2C alkyl or (sic)alkoxy) or together are CH₂; n and p = 0 or 1; m = 1-4; each Ra = H, or 1-12C alkyl or alkenyl; R₇, R₈ and R₉ = H, O (sic), OR₁ or two on adjacent C can be CH₂; R₃ and R₄ = H, Me, Et, CHO or COOH; R₅ and R₆ = H, OH, OMe or O (sic).

USE/ADVANTAGE - The compsns. are used to treat a wide range of tumours, esp. adenocarcinoma of the breast. They are also useful for treating bacterial, viral and fungal infections; to debride selectively skin ulcers; and to heal lesions, acne, warts and inflammatory disorders. These compsns. are less toxic and more effective than the individual components.

0/0

L37 ANSWER 58 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1988-133139 [19] WPIDS

CROSS REFERENCE: 88-292467 [41]; 89-008978 [02]

DOC. NO. CPI: C88-059576

TITLE: Compsns. of catecholic butane derivs. with zinc ions - for treating tumours and skin disorders.

DERWENT CLASS: B05

INVENTOR(S): JORDAN, R T

PATENT ASSIGNEE(S): (CHEM-N) CHEMEX PHARM INC

COUNTRY COUNT: 19

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 8803026 A 880505 (8819)* EN 50

Searcher : Shears 308-4994

08/882499

RW: AT BE CH DE FR GB IT LU NL SE
W: AU DK JP KP KR NO SU
AU 8781724 A 880520 (8833)
EP 288534 A 881102 (8844) EN
R: AT BE CH DE FR GB IT LI LU NL SE
JP 01501794 W 890622 (8931)
US 4880637 A 891114 (9004) 13
EP 288534 B 911218 (9151)
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3775387 G 920130 (9206)
EP 288534 A4 890412 (9348)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8803026	A	WO 87-US2868	871027
EP 288534	A	EP 87-907401	871027
JP 01501794	W	JP 87-506947	871027
US 4880637	A	US 86-925620	861028
EP 288534	A4	EP 87-907401	

PRIORITY APPLN. INFO: US 79-49886 790619; US 82-365781 820405; US
83-465631 830210; US 84-578501 840409; US
85-699923 850211; US 86-924620 861028

AN 1988-133139 [19] WPIDS

CR 88-292467 [41]; 89-008978 [02]

AB WO 8803026 A UPAB: 19940223

Compsn. contg. ionic zinc (II) and at least one catecholic butane of formula (I). R₁, R₂ = H, lower alkyl, lower acyl; R₃, R₄, R₅, R₆, R₁₀, R₁₁, R₁₂, R₁₃ = H or lower alkyl; R₇, R₈, R₉ = H, OH, lower alkoxy or lower acyloxy. More specifically the ionic zinc is in the form of a chelate or a salt, esp. ZnCl₂ and (I) is nordihydroguaiaretic acid (NDGA). The molar ratio of (I):(II) is in the range 10:1 to 1:20.

USE/ADVANTAGE - The compsn. can be used for treating skin disorders such as solid tumours (both benign and malignant), acne, psoriasis, wounds and infections (viral, bacterial and fungal). It does not cause the discomfort of zinc chloride alone or have the side effects of normal anticancer chemotherapy. Specific tumours for which the compsn. is partic. effective include mouse sarcoma-180, malignatn melanoma, human sarcoma-180, squamous cell carcinoma, lung squamous cell carcinoma, breast adenocarcinoma, glioma, glioastrocytoma, renal cell carcinome, Bowenoid carcinoma and basal cell carcinoma.

Dwg.0/0

ABEQ EP 288534 B UPAB: 19930923

A pharmaceutical composition characterised by comprising at least

Searcher : Shears 308-4994

one catecholic butane of the formula (I) wherein R1 and R2 are each independently H, C1-C6 alkyl or C1-C6 acyl; R3, R4, R5, R6, R10, R11, R12 and R13 are each independently H or C1-C6 alkyl; and R7, R8 and R9 are each independently H, hydroxy, C1-C6 alkoxy or C1-C6 acyloxy; and ionic zinc.

ABEQ US 4880637 A UPAB: 19930923

New pharmaceutical compsns. comprise at least 1 catecholic butane of formula (II) and ionic Zn. In (I), R1 and R2 are each H, 1-6Calkyl or acyl; R3-R6 and R10-R13 are each H, 1-6Calkyl; R7-R9 are each H, OH, 1-6C-alkoxy or -acyloxy. Pref. ionic Zn is as Zn salt or chelate of catecholic butane of mol ratio 1:1 to 1:20. Pref. catecholic butane is **nordihydroguaiaretic acid** of formula (I).

USE/ADVANTAGE - Treatment of benign, premalignant and malignant solid tumours, esp. of skin. Dose 2-20 mg/ch₂ solid tumour.

ABEQ EP 288534 A UPAB: 19940120

Compsn. contg. ionic zinc (II) and at least one catecholic butane of formula (I). R1, R2 = H, lower alkyl, lower acyl; R3, R4, R5, R6, R10, R11, R12, R13 = H or lower alkyl; R7, R8, R9 = H, OH, lower alkoxy or lower acyloxy. More specifically the ionic zinc is in the form of a chelate or a salt, esp. ZnCl₂ and (I) is **nordihydroguaiaretic acid (NDGA)**. The molar ratio of (I):(II) is in the range 10:1 to 1:20.

USE/ADVANTAGE - The compsn. can be used for treating skin disorders such as solid tumours (both benign and malignant), acne, psoriasis, wounds and infections (viral, bacterial and fungal). It does not cause the discomfort of zinc chloride alone or have the side effects of normal anticancer chemotherapy. Specific tumours for which the compsn. is partic. effective include mouse sarcoma-180, malignatn melanoma, human sarcoma-180, squamous cell carcinoma, lung squamous cell carcinoma, breast adenocarcinoma, glioma, gliastrocytoma, renal cell carcinome, Bowenoid carcinoma and basal cell carcinoma.

L37 ANSWER 59 OF 70 TOXLIT

ACCESSION NUMBER: 1989:38544 TOXLIT

DOCUMENT NUMBER: CA-110-141554K

TITLE: Pharmacologically active compositions of catecholic butanes with zinc for treatment of skin diseases.

AUTHOR: Jordan RT; Allen LM

SOURCE: (1988). PCT Int. Appl. PATENT NO. 88 01509 03/10/88 (Chemex Pharmaceuticals, Inc.).

PUB. COUNTRY: United States

DOCUMENT TYPE: Patent

FILE SEGMENT: CA

LANGUAGE: English

OTHER SOURCE: CA 110:141554

ENTRY MONTH: 198905

AB Catecholic butanes I (R₁, R₂ = alkyl, acyl; R₃, R₄ = H, Me, Et; R₅, R₆ = H, OH; R₇, R₈, R₉ = H, OH, OR₁) as Zn salts or chelates, or I mixts. with Zn salts, are drugs for the treatment of skin diseases, esp. fungal or bacterial diseases and cancer. A mixt. of ZnCl₂ 46, meso-1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane 11.5, quercetin 11.5, Na ascorbate 7.7, solvent 3.0, and polyethylene glycol 20.4% by wt., applied topically twice, controlled B-16 melanoma and S-180 tumor, in mice.

L37 ANSWER 60 OF 70 MEDLINE

DUPPLICATE 18

ACCESSION NUMBER: 87160921 MEDLINE

DOCUMENT NUMBER: 87160921

TITLE: The effect of modulating the synthesis of arachidonic acid cascade products on HSV lesion recurrence.

AUTHOR: Yates F; Centifanto Y M; Caldwell D R

SOURCE: CURRENT EYE RESEARCH, (1987 Jan) 6 (1) 99-104.

Journal code: DUB. ISSN: 0271-3683.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198707

AB Induction of HSV lesion recurrence may be achieved by a variety of stimuli. Trauma of almost any kind (physical, chemical, electromagnetic and thermal) to the healed primary lesion site has been successful for induction of recurrence. In common with each of these mechanisms is the release of inflammatory mediators (arachidonic acid (AA), complement, kinins, etc.) following trauma. Because blockade of the AA cascade with steroids has been noted to abort HSV skin lesions, and because steroids have numerous side effects making them a poor therapeutic choice in ocular lesions, we decided to test several relatively different types of AA cascade inhibitory drugs in mouse ear HSV recurrence models. In this series of experiments, it was found that topical steroids gave the greatest initial decrease in lesion number (80% fewer than control on day 3 post recurrence induction (PRI), while meclofenamate resulted in the greatest reduction of lesions by day 5 PRI (85% fewer lesions than control and 60% fewer than the steroid treated group). The NDGA treated group exhibited the least reduction in recurrence severity (27% fewer lesions than control on day 5 PRI and 200% more lesions than the steroid group. Chlorpromazine (thorazine) acted roughly equivalent to the steroid treated group by day 5 PRI (70% fewer lesions than the untreated control group). Relative efficacy in lesion reduction between groups by day 5 PRI is: meclofenamate greater than steroid = chlorpromazine greater than NDGA greater than control. Meclofenamate, steroid and chlorpromazine significantly reduced lesions (*p* less than .05) when compared with the saline treated control mice. NDGA did not

Searcher : Shears 308-4994

significantly reduce lesions by day 5 PRI.

L37 ANSWER 61 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
 ACCESSION NUMBER: 1986-318726 [48] WPIDS
 DOC. NO. CPI: C86-138033
 TITLE: Reducing trans-dermal flux of anti neoplastic agent - by addn. of water-soluble zinc cpd., esp. zinc chloride, to enhance skin retention.
 DERWENT CLASS: B07
 INVENTOR(S): ALLEN, L M
 PATENT ASSIGNEE(S): (CHEM-N) CHEMEX PHARM INC; (ACCE-N) ACCESS PHARM INC
 COUNTRY COUNT: 17
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8606586	A	861120	(8648)*	EN	40
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU DE DK FI GB JP NO					
AU 8659066	A	861204	(8718)		
EP 221176	A	870513	(8719)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					
NO 8700001	A	870406	(8720)		
FI 8700013	A	870102	(8740)		
DK 8606349	A	870202	(8751)		
JP 63500171 W		880121	(8809)		
US 4895727	A	900123	(9011)		
AU 9055883	A	900913	(9044)		
EP 506207	A2	920930	(9240)	EN	19
R: AT BE CH DE FR GB IT LI LU NL SE					
EP 506207	A3	930303	(9349)		
EP 221176	B1	940914	(9435)	EN	18
R: AT BE CH DE FR GB IT LI LU NL SE					
DE 3650068	G	941020	(9441)		
EP 872248	A2	981021	(9846)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8606586	A	WO 86-US974	860502
EP 221176	A	EP 86-903757	860502
JP 63500171 W		JP 86-502882	860502
US 4895727	A	US 85-730682	850503
EP 506207	A2	EP 92-201393	860502
EP 506207	A3	EP 92-201393	860502
EP 221176	B1	EP 86-903757	860502
Searcher : Shears 308-4994			

		WO 86-US974	860502
DE 3650068 G		DE 86-3650068	860502
		EP 86-903757	860502
		WO 86-US974	860502
EP 872248	A2 Div ex	EP 86-903757	860502
	Div ex	EP 92-201393	860502
		EP 98-105208	860502

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 506207	A2 Related to	EP 221176
EP 221176	B1 Based on	WO 8606586
DE 3650068	G Based on	EP 221176
	Based on	WO 8606586
EP 872248	A2 Div ex	EP 221176
	Div ex	EP 506207

PRIORITY APPLN. INFO: US 85-730682 850503

AN 1986-318726 [48] WPIDS

AB WO 8606586 A UPAB: 19930922

Additional cites.: - US4122170 US3989816 US3991203 US4411893

US4199576 US41488US4148874 US4362745

Enhancement skin and mucous membrane retention of a pharmacologically active agent (I) comprises adding to (I) a water-soluble Zn cpd., pref. ZnCl₂. (I) is VP-16 (epipodophyllotoxin beta-D ethylidene glucopyranoside-etoposide) VM-26 (epipodophyllotoxin beta-D thenylidene glucopyranoside-teniposide), 4'-demethyl-epipodophyllotoxin, diethylstilbestrol, dithranol, cyclophosphamide, mitomycin, daunomycin, platinum cis-diamine-dichloride, adriamycin or allopurinol.

USE/ADVANTAGE - Retention in the skin is enhanced and prolonged, maximising topical therapeutic effects of pharmaceutical and cosmetic agents and reducing systemic effects of those agents which have systemic activity or toxicity. The specified agents (I) are antineoplastic agents, but the method is more widely applicable e.g. to immunopharmacological agents, antiinflammatory or anti pruritic steroids, topical antifungals, antibacterials or antivirals, antiparasitics, e.g. anthelmintics, pediculicides, anti-acne agents, antipsoriatics, antileprotics, topical anaesthetics, analgesics, counter-irritants, antihistamines, diagnostic agents, vitamins, cosmetic agents and sunscreens.

ABEQ US 4895727 A UPAB: 19930922

Penetration of skin and mucous membrane by a pharmacologically active agent is enhanced and retained, by applying a water-soluble Zn-contg. cpd. which acts to reduce transdermal flux of the agent.

Zn-contg. cpd. comprises ZnCl₂, ZnSO₄, Zn(NO₃)₂, zinc acetate, or zinc stearate. Pharmacological agent comprises e.g. steroid,

Searcher : Shears 308-4994

antiparasitic agent, antileprosy agent, antimetabolite, cell-regulatory agent, immuno-pharmacological agent, allergen, antihistaminic agent, antiinflammatory agent, etc.

ADVANTAGE - Drugs are absorbed and retained for longer periods, overcoming and reducing undesirable systemic toxicity.

ABEQ EP 506207 A UPAB: 19940126

Additional citns.: - US4122170 US3989816 US3991203 US4411893

US4199576 US41488 US4148874 US4362745

Enhancement skin and mucous membrane retention of a pharmacologically active agent (I) comprises adding to (I) a water-soluble Zn cpd., pref. ZnCl₂. (I) is VP-16 (epipodophyllotoxin beta-D ethylidene glucopyranoside-etoposide) VM-26 (epipodophyllotoxin beta-D thenylidene glucopyranoside-teniposide), 4'-demethyl-epipodophyllotoxin, diethylstilbestrol, dithranol, cyclophosphamide, mitomycin, daunomycin, platinum cis-diamine-dichloride, adriamycin or allopurinol.

USE/ADVANTAGE - Retention in the skin is enhanced and prolonged, maximising topical therapeutic effects of pharmaceutical and cosmetic agents and reducing systemic effects of those agents which have systemic activity or toxicity. The specified agents (I) are antineoplastic agents, but the method is more widely applicable e.g. to immunopharmacological agents, antiinflammatory or anti pruritic steroids, topical antifungals, antibacterials or antivirals, antiparasitics, e.g. anthelmintics, pediculicides, anti-acne agents, antipsoriatics, antileprotics, topical anaesthetics, analgesics, counter-irritants, antihistamines, diagnostic agents, vitamins, cosmetic agents and sunscreens.

ABEQ EP 221176 B UPAB: 19941021

A topical pharmaceutical composition for application to the skin or mucous membrane having enhanced skin and mucous membrane penetration and retention comprising a pharmaceutically active agent and an effective amount of a water-soluble zinc-containing compound wherein the pharmacologically active agent is VP-16 (epipodophyllotoxin beta-D ethylidene glucopyranoside-etoposide); VM-26 (epipodophyllotoxin beta-D thenylidene glucopyranoside- teniposide); 4'-demethyl epipodophyllotoxin; diethylstilbestrol; dithranol; cyclophosphamide; mitomycin; daunomycin; platinum cis-diamine-dichloride; adriamycin; allopurinol; 5-fluorouracil, methotrexate or NDGA (nordihydroguaiaretic acid).

Dwg. 0/1

L37 ANSWER 62 OF 70 MEDLINE

ACCESSION NUMBER: 87002662 MEDLINE

DOCUMENT NUMBER: 87002662

TITLE: Effects of inhibitors of arachidonic acid metabolism on intercellular adhesion of SV40-3T3 cells.

AUTHOR: Evans P M; Lanham D F
Searcher : Shears 308-4994

08/882499

SOURCE: CELL BIOLOGY INTERNATIONAL REPORTS, (1986 Sep) 10 (9)
693-8.
Journal code: CRC. ISSN: 0309-1651.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198701

AB Mepacrine, an inhibitor of arachidonic acid mobilisation, and NDGA, a lipoxygenase inhibitor, were found to impair the aggregation of SV40-3T3 cells but the effects could not be unequivocally dissociated from non-specific actions of the drugs. No effect on aggregation was observed even after prolonged exposure of the cells to the cyclooxygenase inhibitors aspirin and indomethacin. These results argue against a possible regulatory role for endogenous AA metabolites in intercellular adhesion of SV40-3T3 cells.

L37 ANSWER 63 OF 70 MEDLINE DUPLICATE 19

ACCESSION NUMBER: 87002016 MEDLINE

DOCUMENT NUMBER: 87002016

TITLE: Inhibition of 12-O-tetradecanoylphorbol-13-acetate-induced induction of Epstein-Barr virus early antigen in Raji cells by some inhibitors of tumor promotion.

AUTHOR: Saito Y; Okamoto H; Mizusaki S; Yoshida D

SOURCE: CANCER LETTERS, (1986 Aug) 32 (2) 137-44.
Journal code: CMX. ISSN: 0304-3835.

PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198701

AB The effects of some compounds, which have been reported to inhibit tumor promotion in vivo, on the induction of the early antigen (EA) of Epstein-Barr virus (EBV) by 12-O-tetradecanoylphorbol-13-acetate (TPA) in Raji cells were examined. The inhibitors of the cascade process involving arachidonic acid, indomethacin, nordihydroguaiaretic acid, phenidone and p-bromophenacyl bromide, effectively inhibited EBV-EA induction by TPA. Two flavonoids, morin and kaempferol also inhibited EA induction. Among antioxidants, butylated hydroxytoluene effectively inhibited EA induction, though alpha-tocopherol did not show any inhibition of EA induction at concentrations of up to 150 micrograms/ml. N-(6-Aminohexyl)-5-chloro-1-naphthalenesulfonamide, a calmodulin antagonist, and esculetin showed inhibitory effects on EA induction, though slight cytotoxicity was observed. L-1-p-Tosylamino-2-phenylethyl chloromethyl ketone, a protease

08/882499

inhibitor, showed cytotoxicity and no specific inhibition of EA induction. Five kinds of steroids, cortisone, hydrocortisone, prednisolone, dexamethasone and fluocinolone acetonide showed no inhibitory effect on EA induction at concentrations of up to 100 micrograms/ml. In addition, the relationship between the inhibition of EBV-EA induction and that of tumor promotion is discussed.

L37 ANSWER 64 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE
20

ACCESSION NUMBER: 86032323 EMBASE
DOCUMENT NUMBER: 1986032323
TITLE: Reversal of feline retroviral suppression
by indomethacin.
AUTHOR: Lewis M.G.; Fertel R.H.; Olsen R.G.
CORPORATE SOURCE: Department of Veterinary Pathobiology, The Ohio State
University Columbus, OH 43210, United States
SOURCE: Leukemia Research, (1985) 9/12 (1451-1456).
CODEN: LEREEDD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
016 Cancer
047 Virology
030 Pharmacology
026 Immunology, Serology and Transplantation
LANGUAGE: English

AB The immunosuppressive effect of feline leukemia virus (FeLV) and its 15,000 dalton envelope protein (p15E) were studied to determine if the mechanism of action was due to an increase in prostaglandin production. We examined the effects of exogenous PGE1 and PGE2 on the normal Con A response of feline peripheral blood lymphocytes (PBL) and found them to be inhibitory. The addition of the cyclooxygenase inhibitor indomethacin to cells incubated with FeLV or FeLV p15E and Con A completely abrogated the viral suppressive effects. This reversal was titratable and time-dependent. Other non-steroidal anti-inflammatory (NSAI) drugs were found to have similar actions. Indomethacin was also able to increase the suppressed Con A response of PBL from FeLV-infected cats. Upon measurement of PGE2 levels from PBL cultured with FeLV, we found a decrease in PGE2 accumulation associated with FeLV presence during the first 24 h of culture. These findings indicate that FeLV does not cause its immunosuppressive effects by increasing PG production and suggests that indomethacin and the other tested NSAI drugs do not produce their effect by PG inhibition.

L37 ANSWER 65 OF 70 MEDLINE

ACCESSION NUMBER: 85303524 MEDLINE
Searcher : Shears 308-4994

08/882499

DOCUMENT NUMBER: 85303524
TITLE: The lipoxygenase pathway in the human NK cell system.
AUTHOR: Jondal M; Kullman C; Lindgren J A; Rossi P
SOURCE: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1985)
184 257-70.
Journal code: 2LU. ISSN: 0065-2598.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198512

L37 ANSWER 66 OF 70 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 85201742 MEDLINE
DOCUMENT NUMBER: 85201742
TITLE: Products of the lipoxygenase pathway in human natural killer cell cytotoxicity.
AUTHOR: Rossi P; Lindgren J A; Kullman C; Jondal M
SOURCE: CELLULAR IMMUNOLOGY, (1985 Jun) 93 (1) 1-8.
Journal code: CQ9. ISSN: 0008-8749.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198509

AB As earlier data suggested the importance of lipoxygenase activation for expression of human NK cell cytotoxicity, four different lipoxygenase inhibitors were tested for suppression of natural killer (NK) cell lysis. All inhibitors were found active at nontoxic concentrations with 50% inhibition at approximately 15 microM for nordihydroguaiaretic acid (NDGA). NK cell lysis could be reconstituted to NDGA-suppressed cells with leukotriene B₄ (LTB₄), the all-trans isomers 6-trans-LTB₄ and 12-epi-6-trans-LTB₄, and 20-COOH-LTB₄. LTB₄ reconstitution was best in the concentration range 1-100 pM and near control levels at both higher and lower concentrations. *Herpesvirus* Ateles-transformed killer T cells could also be inhibited by NDGA. These data indicate that lipoxygenase activity is required for human NK cell lysis and that several different LTB₄-related products can restore NK activity in inhibited cells; they also suggest that the lipoxygenase pathway is present in the killer cell population.

L37 ANSWER 67 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1985:4076 BIOSIS
DOCUMENT NUMBER: BR28:4076
TITLE: NATURAL CYTOTOXIC CELL ACTIVITY ENHANCED BY LEUKOTRIENE B-4 MODULATION BY CYCLOOXYGENASE AND
Searcher : Shears 308-4994

08/882499

AUTHOR(S) : LIPOXYGENASE INHIBITORS.
CORPORATE SOURCE: ROLA-PLESZCZYNSKI M; GAGNON L; SIROIS P
LAB. D'IMMUNOL., DEP. PEDIATRIE, FAC. MED., UNIV.
SHERBROOKE, SHERBROOKE, QUEBEC, J1H 5N4 CAN.
SOURCE: THALER-DAO, H., A. CRASTES DE PAULET AND R. PAOLETTI
(ED.). ICOSANOIDES AND CANCER; SATELLITE SYMPOSIUM OF
THE 2ND INTERNATIONAL CONGRESS ON HORMONES AND
CANCER, ILE DE BENDOR, SEPT. 1983. XIX+289P. RAVEN
PRESS: NEW YORK, N.Y., USA. ILLUS, (1984) 0 (0),
235-242.
ISBN: 0-88167-019-7.
FILE SEGMENT: BR; OLD
LANGUAGE: English

L37 ANSWER 68 OF 70 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 83256539 MEDLINE
DOCUMENT NUMBER: 83256539
TITLE: Leukotriene B4 augments human natural cytotoxic cell activity.
AUTHOR: Rola-Pleszczynski M; Gagnon L; Sirois P
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS,
(1983 Jun 15) 113 (2) 531-7.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198310

AB We have recently shown that leukotriene B4 (LTB4) activates T lymphocytes to become suppressor cells. We now report that LTB4 also augments human natural cytotoxic cell activity against target cells infected with herpes simplex virus. This activity is partially inhibited by the lipoxygenase inhibitor nordihydroguaiaretic acid and the thromboxane synthetase inhibitor OKY-1581, but is augmented by indomethacin. We suggest that LTB4 may play a role in early host defense responses during inflammatory and infectious disease processes.

L37 ANSWER 69 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 83183311 EMBASE
DOCUMENT NUMBER: 1983183311
TITLE: Leukotriene B4 augments human natural cytotoxic cell activity.
AUTHOR: Rola Pleszczynski M.; Gagnon L.; Sirois P.
CORPORATE SOURCE: Lab. Immunol., Unite Rech. Pulm., Fac. Med., Univ.
Sherbrooke, Que. J1H 5N4, Canada
SOURCE: Biochemical and Biophysical Research Communications,
(1983) 113/2 (531-537).

Searcher : Shears 308-4994

CODEN: BBRCA
 COUNTRY: United States
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 037 Drug Literature Index
 029 Clinical Biochemistry
 026 Immunology, Serology and Transplantation
 047 Virology

LANGUAGE: English

AB We have recently shown that leukotriene B₄ (LTB₄) activates T lymphocytes to become suppressor cells. We now report that LTB₄ also augments human natural cytotoxic cell activity against target cells infected with herpes simplex virus. This activity is partially inhibited by the lipoxygenase inhibitor nordihydroguaiaretic acid and the thromboxane synthetase inhibitor OKY-1581, but is augmented by indomethacin. We suggest that LTB₄ may play a role in early host defense responses during inflammatory and infectious disease processes.

L37 ANSWER 70 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD

ACCESSION NUMBER: 83-27628 DRUGU P B

TITLE: Mechanisms of Fever.

AUTHOR: Hellon R; Townsend Y

LOCATION: London, United Kingdom

SOURCE: Pharmacol.Ther. (19, No. 2, 211-44, /1982/1983/) 20

Fig. 3 Tab. 201 Ref.

CODEN: PHTHDT ISSN: 0163-7258

AVAIL. OF DOC.: National Institute for Medical Research, London, NW7, England.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 83-27628 DRUGU P B

AB The mechanisms of fever are reviewed with respect to endogenous pyrogens and their biosynthesis, metabolism, release and site of action, central mediators of fever, the fever response in pregnant and neonatal animals and the survival value of the fever response. Endogenous pyrogens appear to be proteins released by leukocytes with a site of action in the hypothalamus. Candidates for the central mediator of fever include prostaglandins, monamines and proteins.

ABEX Many clinical conditions can give rise to fever including bacterial, viral, protozoal, and fungal infections, malignancies, immunological diseases and inflammatory disorders. Endotoxins from gram negative bacteria induce a febrile response. However, gram positive bacteria and viruses do not have an endotoxin but induce the synthesis of an endogenous pyrogen (EP) by being phagocytosed. EP is derived from leukocytes, especially

Searcher : Shears 308-4994